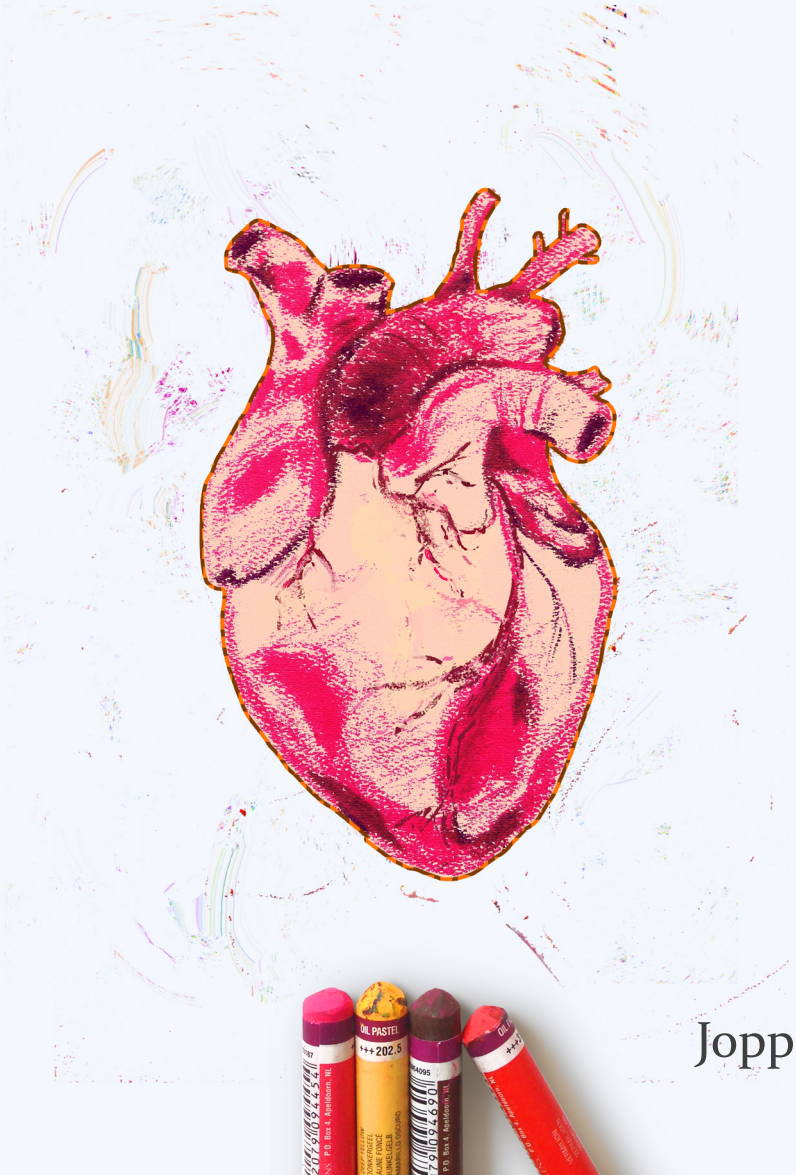
Measuring the Quality of Care for Patients with Acute Coronary Syndrome: A Process Approach



Joppe Tra

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Measuring the quality of care for patients with acute coronary syndrome: a process approach

ACADEMISCH PROEFSCHRIFT

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	dr. I. van der Wulp

If you can't describe what you are doing as a process,
you don't know what you're doing.

W. Edwards Deming

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Chapter 1

Introduction

This introductory chapter provides background information on the main topics and research questions of this thesis: acute coronary syndrome (ACS), its prevention and management, and measuring the quality of care.

ACUTE CORONARY SYNDROME

ISCHAEMIC HEART DISEASE

In the year 1772, the English physician William Heberden described 20 patients with a 'painful and most disagreeable sensation in the breast' in *Transactions in the Royal College of Physicians of London*.[1] He named the condition 'Angina Pectoris'.[2] Although he might have discounted the heart as a cause for angina pectoris, Heberden's observations eventually led to the discovery of ischaemic heart disease.

Nowadays, ischaemic heart disease is the leading cause of death in the world.[3] In Europe, almost 24% of all deaths is caused by ischaemic heart disease, totalling 2.1 million deaths each year. Although this percentage will decrease slightly to 20.5% in the next 15 years,[4] the burden of disease will remain immense. The most common ischaemic heart disease is ACS.

WHAT CAUSES ACUTE CORONARY SYNDROME?

Three coronary arteries located on the outside of the heart provide the heart muscle tissue, or myocardial tissue, with vital glucose- and oxygen-rich blood. In case of an ACS, this blood provision is reduced or cut off for a prolonged time, usually due to the rupture of an atherosclerotic plaque in the wall of one or more of the coronary arteries.[5] The reduction or deprivation of glucose and oxygen rich blood causes ischaemia, which in turn can result in tissue necrosis. The reduction in blood flow can lead to several signs and symptoms in patients, such as chest pain (angina pectoris), radiation of this pain to the upper extremities, nausea and excessive sweating.[6] However, signs and symptoms may vary. For example, women, elderly, patients with diabetes mellitus, and patients with a history of heart failure tend to present more often without typical chest pain or discomfort, and more often with abdominal pain or muscle cramps in the jaw.[7] Also, several other conditions should be considered in the differential diagnoses, e.g. pericarditis. Consequently, additional diagnostics are required.

CLINICAL MANIFESTATIONS AND DIAGNOSIS

In diagnosing acute coronary syndrome, three clinical manifestations can be distinguished based on electrocardiogram changes and biomarker values.[8] As a result of ischaemia, the electrophysiological field of the myocardial tissue changes, which shows on the electrocardiogram as deviations in a particular part of the signal (ST-segment). Biomarkers (i.e. troponin, creatine-kinase (CK) and creatine-kinase muscle-brain (CK-MB)) are enzymes which are released in the blood stream as a result of myocardial tissue necrosis.[8] When the electrocardiogram shows an elevation of the ST-segment and the biomarker values are increased, the clinical manifestation of ACS is named ST-segment elevation myocardial infarction (STEMI). This is generally the result of a complete coronary artery occlusion.

When there is no complete occlusion of the coronary artery, the blood flow can still be heavily reduced, resulting in the release of biomarkers though the electrocardiogram may show no characteristic changes. This manifestation of ACS is named Non-ST-segment Elevation Myocardial Infarction (NSTEMI).

When the blood flow is reduced but still sufficient for the myocardial tissue to survive, no biomarkers are released and no characteristic changes on the electrocardiogram are present. However, these patients may experience typical symptoms such as chest pain during rest. In these cases, the manifestation of ACS is named Unstable Angina pectoris (UA).

Of all patients with ACS, 47% is diagnosed with STEMI and 48% with NSTEMI or UA, while 5% has an undetermined electrocardiogram pattern.[9] An overview of the three manifestations is provided in Figure 1.

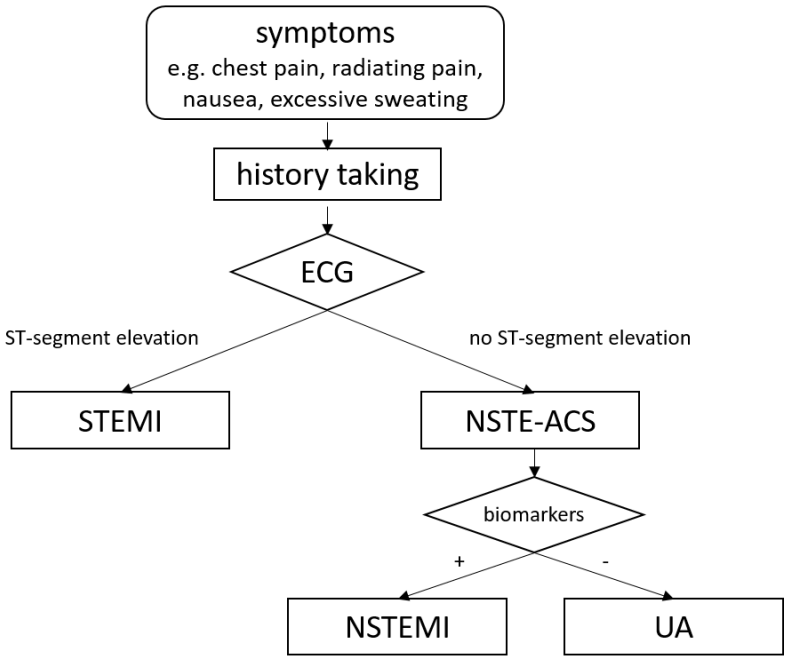

Figure 1 The three clinical manifestations of acute coronary syndrome

FREQUENCY AND SEVERITY OF ACS

Internationally

The number of patients with an ACS decreased in the last decade. The incidence of STEMI and NSTEMI was 28% lower in 2008 than in 2000 (208 and 287 cases per 100,000 person-years respectively).[10]

Patients with an ACS have a higher risk of developing other life-threatening cardiac complications such as cardiogenic shock, heart failure[11] or cardiac arrhythmias[12]. Consequently, acute coronary syndrome increases the risk of dying both on the short as well as the longer term. Of the patients with STEMI who are treated at the hospital, 4.6% die during admission, while an additional 4.5% die within the six months after hospital discharge.[13] Patients diagnosed with NSTEMI and UA are more likely to survive as in-hospital mortality and mortality after 6 months are 2.2% and 3.3% respectively. For STEMI, the in-hospital mortality decreased, while for NSTEMI and UA, the 6-month mortality decreased over the years.[13]

Despite improvements in survival, ACS remains a major cause of mortality and morbidity in the world and further improvements in its management are imperative. Although recent numbers are lacking, the annual health care costs have been estimated at billions per country.[14]

The Netherlands

In the Netherlands, 78 people are hospitalized with STEMI or NSTEMI every day.[15] The mortality rates due to ACS have been decreasing slightly over the years.[16] In 2014, over 5,000 people died from STEMI or NSTEMI (Table 1).

Table 1 Deaths due to acute myocardial infarction in the Netherlands over the years 1996-2015

Year	1996	2000	2005	2013	2014	2015
Death due to AMI	15,145	12,898	9,445	5,688	5,301	5,403

AMI = acute myocardial infarction. Source: Statline, Statistics Netherlands, Den Haag/Heerlen. Updated 18-06-2017.

However, the costs of the management of patients with cardiovascular diseases have increased by 7.6% between 1999 and 2010. The total costs for patients with ischaemic heart disease were 2.1 billion euro in 2011, or 2.3% of the total health care costs.[17] ACS therefore represents an enormous societal and financial burden, and aggressive and elaborate management is warranted.

PREVENTION AND MANAGEMENT OF ACS

Much research has been done on the prevention and management of cardiovascular disease, including ACS. The prevention starts with the promotion of a general healthy lifestyle and environment, e.g. not smoking and eating healthy.[18] In addition, primary care focusses on monitoring people at increased risk of developing ACS, such as people with hypercholesterolaemia, high blood pressure or people who smoke. These risk factors can be controlled by interventions such as prescribing blood pressure lowering medication or advising on smoking cessation. When increased primary prevention efforts result in improved risk factor control (e.g. lower blood pressure), it is expected that the incidence of ACS will also decrease.[19, 20]

When patients experience symptoms of ACS, it is essential that they recognize these, acknowledge their severity, and contact a health care provider as soon as possible. The care professionals who come into contact with the patient first have to assess the likelihood that the patient has an ACS.[21] This is performed by means of history taking, electrocardiogram recording and biomarker measurement (at the hospital). After the diagnosis of ACS has been established, it is vital to assess the patient's risk of heart failure, recurrent ACS or mortality. The management strategy depends on that risk, and differs between the three manifestations of ACS.[22, 23]

ACUTE MANAGEMENT OF STEMI

In the era of Heberden, there was little understanding of the pathophysiological mechanism of ACS. Patients were therefore 'treated' with bed rest until their chest pain was over.[24] Nowadays in patients diagnosed with STEMI, it is commonly known that restoring the blood flow to the myocardial tissue (reperfusion) as soon as possible is of vital importance.[25] Medication is administered immediately to reduce the blood clot formation e.g. acetylsalicylic acid and a P2Y12 receptor inhibitor. Subsequently, a coronary angiography is performed to identify the location of the stenosis and the severity of blood flow reduction in the coronary arteries. Angiography is an X-ray based technique with which the coronary arteries are visualized by means of a radioactive, fluorescent liquid that is injected into the arteries. When severe coronary stenosis is detected, the preferred reperfusion treatment is percutaneous coronary intervention (PCI).[26] PCI is a minimally invasive (catheter based) technique first introduced by Swiss radiologist Andreas Grüntzig. With this technique, a balloon is placed and inflated on the location of the coronary stenosis, which forces the artery open.[27] Grüntzig used a technique that was previously applied to open an occlusion in the arteries of the leg by Charles Dotter,[28] hence the Dutch word for PCI 'dotteren'.

It is essential to treat STEMI patients with PCI as soon as possible, as the likelihood of dying after STEMI increases with 7% for every 30 minute increase in the time between symptom onset and reperfusion.[29] The general consensus is that patients should receive PCI within 90 minutes from first (para)medical contact. While the time dependency of pharmacological reperfusion therapy (thrombolysis) was already confirmed by a meta-analysis in 1994,[30] it was not until the year 2000 that a similar time dependency was demonstrated for PCI by Cannon and colleagues[31].

When revascularization by means of PCI is not possible, e.g. due to multiple occluded arteries, patients are reviewed in a multidisciplinary heart team[32] and referred for optimal pharmacological management or coronary artery bypass grafting (CABG). In this surgical procedure, the occlusion in the coronary artery is bypassed by grafting a blood vessel which is commonly excised from the patient's arm or leg.

ACUTE MANAGEMENT OF NSTEMI AND UA

While coronary angiography and PCI are indicated for most patients with STEMI, not all patients with NSTEMI or UA benefit from it as the population is more heterogeneous in terms of risk and prognosis.[22] Therefore it is important for these patients to weigh the risk and benefit of invasive treatment against the risk of reinfarction or death by means of validated risk scoring instruments.[33] When the estimated risk of reinfarction

or death is low or the estimated risk of adverse outcomes after a PCI procedure is high, pharmacological therapy is provided to prevent disease progression.[22] In case the patient is assigned to PCI treatment, the procedure should be initiated within two hours for very high risk, within 24 hours for high risk and within 72 hours for other patients.[22]

SECONDARY PREVENTION

After the immediate treatment of ACS, the risk of a recurrent ACS is increased due to inflammation in the plaque.[34] It is essential to prevent recurrence of ACS by means of additional pharmacological therapy, risk factor control and lifestyle changes.[35] In order to reduce the risk of blood clot formation, medication is provided to inhibit platelet aggregation, e.g. a combination of acetylsalicylic acid and a P2Y12 receptor inhibitor. Moreover, statins are prescribed to lower cholesterol (one of the ACS risk factors) and to reduce the inflammation in the atherosclerotic plaque, consequently limiting the chances of a plaque to rupture.[34] Finally, beta blockers and Angiotensin converting enzyme (ACE)-inhibitors are prescribed to lower the blood pressure.

In addition to medication for secondary prevention, specialized cardiac rehabilitation programs which focus on physical exercise, lifestyle and psychosocial health after an ACS are provided.[35]

THE ORGANISATION OF ACS CARE IN THE NETHERLANDS

Many care providers are involved in the prevention and management of ACS in the Netherlands. General practitioners monitor people at an increased risk of ACS. When an acute coronary syndrome occurs during business hours, patients call or visit their general practitioner. Outside of business hours, general practitioners cooperate in after-hours clinics. The policy for general practitioners when they suspect an ACS is to call an ambulance immediately.[36] Alternatively, the patient can call an ambulance directly through the national emergency phone number (112) or go to the emergency department of a hospital. The emergency medical services in the Netherlands (the combination of dispatch centres and ambulances) are organised in 25 self-dispatching ambulance regions (Figure 2).

For ambulances, the policy for patients suspected of STEMI is to make a tentative diagnosis based on careful evaluation of the patient's signs and symptoms and an electrocardiogram performed on-site. In case a STEMI is confirmed by the electrocardiogram, acute care medication is provided (e.g. acetylsalicylic acid and P2Y12 inhibitor) and the patients is immediately transported to a PCI capable hospital to undergo primary PCI.[37] PCI is the reperfusion therapy of choice in the Netherlands

as it has been shown to be superior compared to pharmacological reperfusion therapy (thrombolysis or fibrinolysis).[38] At the start of our research (2013), 30 PCI capable hospitals served a population of 16.8 million people in the Netherlands. When compared to other European countries, this can be considered good geographical accessibility.[39] Patients with NSTEMI or UA are transported to the nearest hospital with appropriate care facilities (e.g. a coronary care unit).

Figure 2 Ambulance regions and PCI centres (dots) in the Netherlands in 2013 (Sources: www.zorgatlas.nl, AZN, NVVC white lists for PCI centres)

Secondary prevention after ACS is initially provided in cardiac rehabilitation programs of hospitals in the Netherlands.[40] These multidisciplinary programs consist of modules for physical exercise, psychological health, social health and lifestyle provided by cardiologists, nurses, physical therapists, psychologists, social workers and dieticians.[35] After participation in the program, secondary prevention therapy is continued during regular checks with a cardiologist and/or cardiac care nurse, and eventually taken over by the general practitioner.

VARIATION

The above description of the management of ACS in a care chain is based on perfect application of the cardiology guidelines. However, not all of these steps are taken for all patients with ACS, resulting in variation in its management. This variation can be caused by medical reasons and/or patient preference, but some variation is unwarranted. This unwarranted variation potentially affects the quality of care (and thereby patient outcomes)[41] and is therefore of interest for the field of health services research.

THE QUALITY OF CARE FOR PATIENTS WITH ACS

According to the Institute Of Medicine and the World Health Organization, health care should be effective, efficient, accessible, acceptable, patient-centred, equitable and safe.[42] In this thesis, the focus will be on the effectiveness of the care for patients diagnosed with ACS. Effectiveness is defined as the extent to which the delivered health care is adherent to an evidence base and results in improved outcomes for patients, e.g. reduced morbidity and mortality, and an improved quality of life.[41] Adherence to the evidence base is important to reduce under- and overuse of interventions in health care as new evidence comes to light. However, the evidence base is ever growing. In order to keep up with all the developments within the medical specialism of cardiology, one would need to read 75 papers on trials and 11 papers on systematic reviews every day.[43] The evidence is therefore periodically summarized in evidence-based guidelines.[42]

GUIDELINES

Use of these guidelines standardizes care and assists physicians in making treatment decisions for patients with ACS. One of the key developers of cardiology guidelines in Europe is the European Society of Cardiology (ESC). The first ESC guideline for the management of ACS was presented in 1996.[44] Since then, multiple guidelines on the management of STEMI and NSTEMI/UA, and specifically on prevention and revascularization have been published. These guidelines are created by means of a review of the literature, of which the findings are synthesized by a task force.[45] In general, adhering to the guidelines can be considered good quality of care, although physicians can always deviate from guidelines with sound medical rationale. However, creating evidence-based guidelines does not guarantee that care providers also know of, use and apply them in clinical practice. Suboptimal implementation can result in unwarranted practice variation, e.g. patients in one hospital are treated differently than in another hospital without medical rationale for this difference. Therefore, it

is important to monitor and improve guideline adherence, e.g. by means of quality indicators.

QUALITY INDICATORS

The purpose of quality indicators is to measure, evaluate and ultimately improve the quality of care, and/or to provide transparency in the quality of care for accountability purposes. The quality of health care can be evaluated on its structures, processes and outcomes.[46] In order to improve the outcomes of care, it is essential to have an organisational structure in which appropriately trained health care professionals are in the right place at the right time. In addition, the care processes should be in accordance with the latest scientific evidence. Adhering to these two criteria should eventually lead to optimal patient outcomes.

Development of quality indicators is preferably performed by combining a systematic review of the literature with consensus meetings.[47] The literature review is used to identify all possible evidence-based aspects of the care, resulting in a large pool of potential quality indicators. This pool needs to be reduced as the administrative burden in hospitals is already high and can take resources away from patient care. In one or more consensus meetings, an expert panel therefore selects a number of indicators which they consider as most useful, reliable and valid in evaluating the quality of care. Only the quality indicators with satisfactory ratings on all criteria are included in the final indicator set. Because the guideline development should already include a systematic literature review and an expert panel, the development of quality indicators can be integrated in this process. Since guidelines are generally lengthy manuscripts with numerous recommendations, only the recommendations with the strongest link to patient outcomes and measurable in practice should be selected to serve as quality indicator.[47] The synthesis from scientific evidence to quality indicators is summarized in Figure 3.

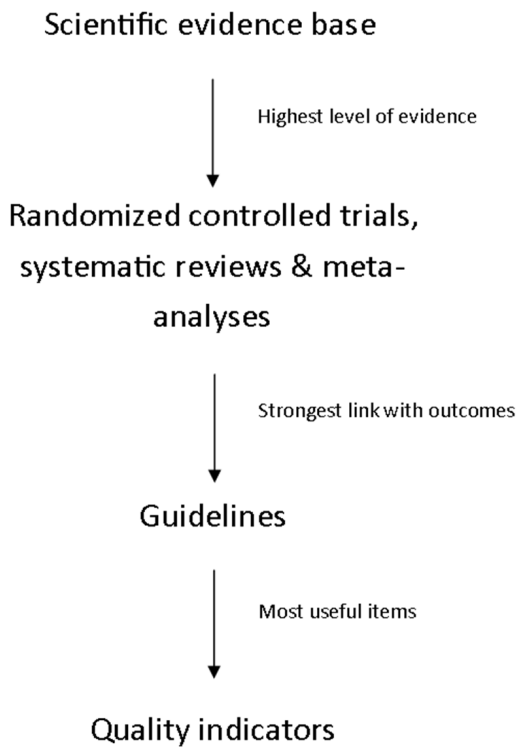

Figure 3 The synthesis of scientific evidence into quality indicators

Quality indicators can be informative for many stakeholders in health care i.e. clinicians, hospital executive boards, health insurance companies, the health care inspectorate and patients.[48]

Clinicians can use their performance on indicators to monitor and improve their practice and identify unwarranted practice variation within their organisation, assisted by quality officers at the hospital (performance feedback). By comparing their practice to other, comparable care providers (benchmarking), they can identify suboptimal performance. Benchmarking has been identified as an excellent tool to improve practice.[49] Ideally, measuring quality indicators leads to health care organisations that are aiming to continuously improve their practice, i.e. learning organisations.[50]

The hospital executive board is ultimately responsible for the quality of the care provided in the hospital. Quality indicators offer the executive board of a hospital a way to monitor the quality performance of various hospital departments, usually through quality officers. In organisational management, these indicators can be a valuable addition to other performance indicators, e.g. financial or human resource indicators.

Besides clinicians and the hospital itself, the information derived from quality indicators can also be of use to health insurance companies. The Dutch health care system is designed with a quality role for the health care insurance companies in mind. These companies should selectively purchase care that conforms to their predefined quality standards. So far, there is little reliable and valid information pertaining to health care quality available.

Furthermore, the health care inspectorate (IGZ) can use the indicators to monitor performance and safety of the provided care and intervene when it falls below a certain threshold and patients might be at risk.

Finally, when the right content is presented in the right form, patients should be able to use information from indicators to make an informed choice for a care provider when they require care.[51] In the Netherlands, this role is facilitated by the Netherlands Health Care Institutes (Zorginstituut).

QUALITY IMPROVEMENT

The overarching goal of monitoring the quality of care is to facilitate continuous quality improvement. Monitoring is therefore a vital part of many quality improvement models, e.g. Six Sigma (define, measure, analyse, improve, control), Lean (reducing the number of process steps) and Plan-Do-Check-Act.[52] The latter is one of the most commonly used methods for quality improvement in health care. By monitoring the current performance, targets for improvement can be identified and the most appropriate improvement strategy can be identified by in-depth analyses of the results on the quality indicators (Plan). When carrying out the plans (Do), it is vital to monitor the effectiveness of the quality improvement efforts (Check). The information from quality indicators enables measurement of the effectiveness of the quality improvement efforts and adjustment where required (Act). Afterwards, new targets for quality improvement are defined and the cycle continues.

In health care, the ultimate goal of quality improvement is to improve patient outcomes. However, a sole focus on outcomes offers no direction for improvement, as it is unclear what might have contributed to the improved patient outcomes. Thus, measuring structures and processes provides insight in where improvements can be made. In the management of ACS, process improvements have been linked to improvements in outcomes[53,54] and therefore provide a useful approach in improving the care. Improving the structure and process of care will ideally lead to improved outcomes. Before improvement is possible, the current quality of the process of care should first be monitored.[55]

VMS SAFETY MANAGEMENT PROGRAM

In 2004, a report of Shell Netherlands CEO Rein Willems (expert in safety management) recommended several ways to improve hospital care in the Netherlands.[56] Furthermore, a report on adverse events in 2007 indicated that 5.7% of the patients treated in hospitals experienced an adverse event[57] i.e. an unintended injury related to medical management instead of the disease.[58] As a result, the Netherlands Federation of hospitals (NVZ), the Netherlands Federation of University Medical Centres (NFU), the Dutch nursing society (V&VN) and Netherlands Order of Medical Specialists (OMS, currently known as FMS) initiated a safety program. The program focussed on ten clinical themes (and eventually an eleventh was added) and on implementing a safety management system to reduce adverse events. A safety management system is a hospital system to continuously identify risks, report incidents, improve performance, create a safety culture, and document, evaluate and adapt safety policy.

One of the clinical themes was 'Optimal care for acute coronary syndromes'. For each theme, a practice guide was developed by an expert panel from the respective field. The practice guide for ACS management highlighted important recommendations from the ESC guidelines and contained a set of five quality indicators to evaluate the structure, process and outcome of care. To evaluate the **structure** of ACS care, all hospitals were required to have a policy to refer all ACS patients for cardiac rehabilitation. The **process** was evaluated by three quality indicators: the number of STEMI patients who were treated with PCI within 90 minutes from first medical contact; the number of NSTEMI/UA patients in which validated cardiac risk scores were used to decide on the type of treatment to initiate; and the number of ACS patients in which the guideline recommended secondary prevention medication was prescribed at discharge. Finally, the **outcome** of care was evaluated by determining the number of patients who died within 30 days after being diagnosed with ACS (for internal use only). The quality indicators are shown within the care pathway of ACS in Figure 4.

The intention of this safety program was that hospitals would upload the results on these quality indicators to a national online tool, in order to enable benchmarking of performance. However, this challenge proved too big, resulting in a lack of national data and a premature termination of the online tool. Consequently, there was no information about the performance of hospitals on the VMS quality indicators. To obtain this information, independent research institutes (EMGO+ and NIVEL) were asked by the Dutch Ministry of Health, Welfare and Sports to evaluate the effects of the VMS program.

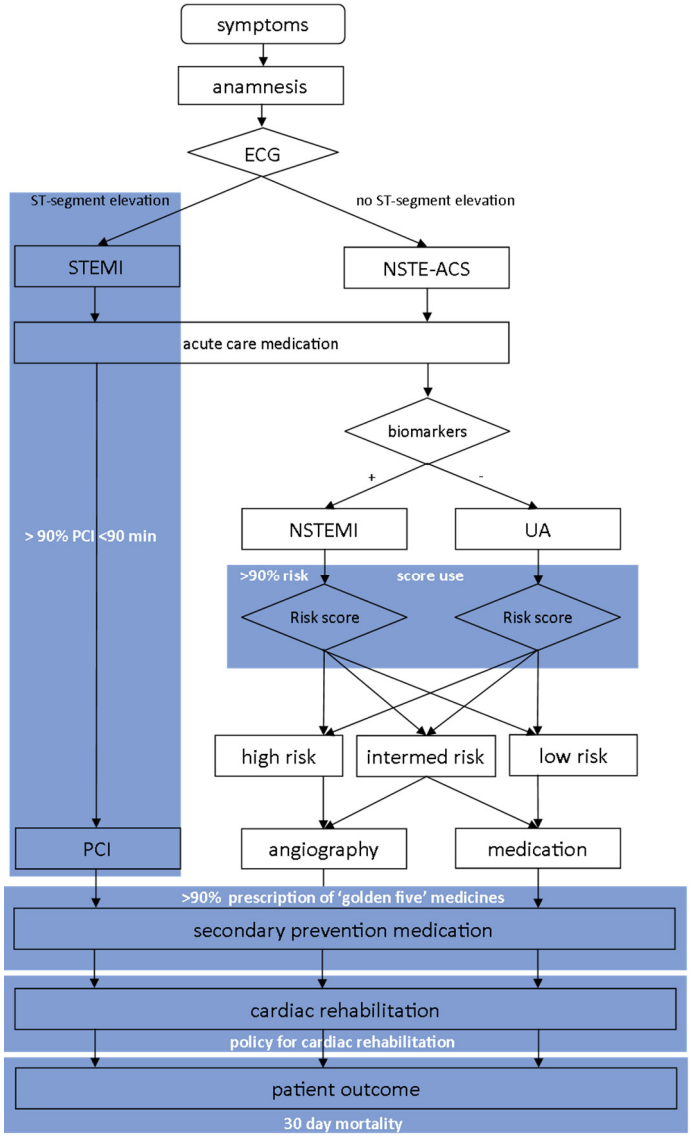

Figure 4 The usual management of patients with acute coronary syndrome and the VMS quality indicators. For overview purposes, coronary artery bypass grafting was not included as a treatment option. ACS = acute coronary syndrome; ECG = electrocardiogram; STEMI = ST-segment elevation myocardial infarction; NSTE-ACS = non-ST-segment elevation acute coronary syndrome; NSTEMI = non-ST-segment elevation myocardial infarction; UA = unstable angina; intermed = intermediate; golden five = acetylsalicylic acid, P2Y12 receptor inhibitor, statin, beta blocker and angiotensin converting enzyme inhibitor. VMS ACS quality indicators are highlighted in blue.

FOCUS AND OBJECTIVES

Although the quality of care for patients with ACS has improved tremendously over the years, many patients still die as a result of ACS. Consequently, small improvements in the quality of care can result in large positive effects on patient outcomes on a national level. In the management of ACS, process improvements have been linked to improvements in outcomes[53, 54] and therefore provide a useful approach in improving the care. Furthermore, several interventions to improve ACS care processes were previously described in scientific literature.[59, 60]

However, there is little information about the quality of the care process in the management of ACS patients in the Netherlands. Previous initiatives to obtain information about the quality of the care process have predominantly been local [61, 62] or regional [63, 64] and indicate that there is ample room for improvement. In addition, there is no national data ACS registry,[65] in contrast to other countries (e.g. Sweden, United Kingdom, and the United States[66]). Due to the premature termination of the online VMS tool to upload the results of the quality indicators, there is no information on the potential room for improvement and unwarranted practice variation in Dutch ACS care.

Therefore, in this thesis the quality of ACS management is evaluated by measuring two process quality indicators with an established association with patient outcomes from the VMS quality improvement program: timely invasive treatment[31,] and prescription of secondary prevention medication at discharge[53]. These quality indicators were subsequently adapted to match the ESC guidelines more closely and were further specified to match Dutch Cardiology practice (e.g. the start and end of the treatment delay indicator).

The research questions of the thesis are:

1) to what degree are the guideline recommendations for minimizing treatment delay in STEMI and the prescription of secondary prevention medication adhered to in Dutch hospitals?

2) to what extent is there unwarranted process variation in the performance of hospitals on these quality indicators?

3) what interventions are most effective for improving the ACS care process?

These research questions are described in several chapters. In **chapter 2** an overview of the literature and the design of a national study to evaluate the quality of the process of ACS management by means of patient record review are presented. In **chapter 3** the treatment delay and associated factors for patients with STEMI are explored. **Chapter 4** describes the effects of data and definition issues on the treatment delay quality indicator scores. In **chapter 5** a qualitative analysis (by means of a multiple case study) of the acute processes of care for STEMI patients in more detail, including accelerating factors as perceived by health care providers. In **chapter 6** the guideline adherence and associated factors in prescribing secondary prevention medication at discharge from the hospital are explored. **Chapter 7** contains a systematic review of interventions to improve guideline adherence in the process of ACS care and their effectiveness. Finally, in **chapter 8** the main findings are discussed; the VMS ACS quality indicators are reflected upon; (methodological) considerations are presented; and lessons learned are summarized in recommendations for clinical practice and future research.

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Chapter 2

Monitoring guideline adherence in the management of acute coronary syndrome in hospitals: design of a multicentre study

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ABSTRACT

Background: Increasing guideline adherence in the management of acute coronary syndrome (ACS) in hospitals potentially reduces heart failure and mortality. Therefore, an expert panel identified three guideline recommendations as the most important aims for improvement in ACS care, i.e. timely invasive treatment, use of risk scoring instruments and prescription of secondary prevention medication at discharge.

Aims: This study aims to evaluate in-hospital guideline adherence in the care of patients diagnosed with ACS and to identify associated factors.

Methods: The study has a cross-sectional design. Data are collected in 13 hospitals in the Netherlands by means of retrospective chart review of patients discharged in 2012 with a diagnosis of ACS. The primary outcomes will be the percentages of patients receiving timely invasive treatment, with a documented cardiac risk score, and with a prescription of the guideline-recommended discharge medication. In addition, factors associated with guideline adherence will be studied using generalised linear (mixed) models.

Discussion: This study explores guideline adherence in Dutch hospitals in the management of patients diagnosed with ACS, using a data source universally available in hospitals. The results of this study can be informative for professionals involved in ACS care as they facilitate targeted improvement efforts.

BACKGROUND

Patients diagnosed with an acute coronary syndrome (ACS) have a high risk of dying from their condition. Mortality rates differ for the three clinical manifestations of ACS: ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina (UA).[1] The symptoms of ACS are usually caused by the same pathophysiological mechanism, i.e. coronary stenosis. However, the differences in severity of coronary stenosis and mortality have led to differences in the management of ACS.[2, 3]

Improved management strategies for patients diagnosed with ACS have led to a decrease in mortality rates in the past years.[4-6] For patients with STEMI the strategy progressed from acute pharmacological intervention (thrombolysis) to immediate percutaneous coronary intervention (PCI).[7] In the management of NSTEMI and UA patients, risk scoring instruments were developed and implemented to estimate patients' future risk of major adverse cardiac events in order to weigh the risks and benefits of invasive treatment.[8] Independent of the type of ACS, prescribing secondary prevention medication further reduces morbidity and prevents additional episodes of ACS.[9] Using the aforementioned strategies increases patients' chances of survival[10, 11] and these strategies are therefore incorporated in international cardiology guidelines[12, 13].

However, previous studies reported that not all patients are treated according to these guideline-recommended strategies.[14, 15] For example, patients with higher age, female sex, prior heart failure, renal insufficiency or coronary artery bypass graft (CABG) surgery during admission were less likely to receive guideline-recommended discharge medication.[16] Also, variation in guideline adherence between hospitals has been reported.[10] To identify room for improvement in the management of ACS, it is imperative to monitor guideline adherence and to identify associated factors.

The objective of this study is therefore to determine the degree of ACS guideline adherence in Dutch hospitals. A Dutch expert panel identified timely invasive treatment, use of cardiac risk scoring instruments and prescribing guideline-recommended discharge medication as the most important aims for improvement in ACS care. A secondary objective of this study is to explore patient and hospital characteristics associated with guideline adherence. In the present paper, the design of the study will be outlined.

RESEARCH QUESTIONS

To what degree are:

- patients diagnosed with STEMI treated with PCI within 90 min of first (para) medical contact?

- cardiac risk scoring instruments used in the management of patients diagnosed with NSTEMI/UA?

- the recommended medicines for secondary prevention prescribed to patients diagnosed with ACS at discharge from the hospital?

Additionally, what patient and hospital characteristics are associated with guideline adherence?

METHODS/DESIGN

DESIGN

The study has a cross-sectional design.

SETTING

In the Netherlands 30 out of the 91 hospitals offer PCI, of which 16 also provide CABG surgery. The three guideline recommendations monitored in the present study were identified from the European Society of Cardiology guidelines by an expert panel consisting of cardiologists, an emergency department medical resident, an intensive care/cardiac care nurse and health care scientists. Adherence to these three recommendations is measured over 2012, the last year of a national quality improvement program. The program aims to decrease in-hospital mortality caused by ten high-risk patient safety threats, including ACS.[17]

SELECTION OF HOSPITALS

The study is being conducted in 13 hospitals, selected by means of a multi-stage random sampling procedure. Initially six PCI-capable and six non-PCI-capable hospitals with a cardiology department were randomly selected from a pool of 40 randomly selected hospitals. Three PCI-capable hospitals declined participation, for which three additional PCI-capable hospitals were selected. Because the number of STEMI patients was relatively small, an additional PCI-capable hospital was selected. The hospitals are located in 7 of the 12 Dutch provinces, with bed capacities ranging between 200 and 1200 beds (Table 1).

Table 1 Characteristics of hospitals included in the study

Hospital ID	1	2	3	4	5	6	7	8	9	10	11	12	13
Type	Gen	Gen	Gen	Teach	Teach	Gen	Teach	Teach	Teach	Acad	Teach	Teach	Acad
Beds	200-400	200-400	200-400	400-600	400-600	800-1000	600-800	600-800	600-800	600-800	1000-1200	800-1000	800-1000
PCI	No	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
CABG	No	No	No	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes

Gen = General hospital; Teach = Tertiary teaching hospital; Acad = Academic hospital; PCI = Percutaneous Coronary Intervention; CABG = Coronary Artery Bypass Graft surgery

Due to privacy reasons, bed capacity is categorized and the province per hospital is not included

DATA COLLECTION

The data are collected by means of retrospective chart review of electronic and/or paper-based medical, nursing and catheterisation laboratory charts of patients discharged between January 1st and December 31st, 2012. Monthly, potential study charts are selected from the hospital billing system using diagnosis-treatment combination codes. Charts of patients discharged with a confirmed diagnosis of ACS (indicated in the discharge letter) are considered for inclusion (Fig. 1). When the discharge diagnosis is unclear, the chart is discussed with a cardiologist or other attending physician working in the field of cardiology. Charts of patients without a discharge diagnosis of ACS, a secondary ACS (e.g. due to anaemia), elective procedures, missing or uninformative charts, and charts of patients under the age of 18 years are excluded from the study. Moreover, additional exclusion criteria were defined for each process indicator separately. For timely invasive treatment, charts of STEMI patients not going for acute PCI are excluded. For use of risk scoring instruments, charts of patients transferred from another hospital are excluded. For discharge medication, charts of patients who were transferred to another hospital, patients who died during their admission or received palliative treatment are excluded. If the monthly number of charts exceeds the screening capacity, screening of the charts is performed in chronological order of discharge representing STEMI and NSTEMI/UA equally, and terminated when the chart abstractors are practically unable to screen additional charts.

In two hospitals, the pre-selection procedure based on the hospital billing system is not possible. Therefore, in one hospital the pre-selection of charts is performed by requesting all charts of patients with a suspected or confirmed diagnosis of ACS through the cardiology department's secretariat. In the other hospital, local hospital regulations require that patients with a suspected ACS are informed about the study and asked to give informed consent before their chart can be considered for inclusion.

Due to the declined invitations and deviations in inclusion procedures, data collection in 5 hospitals will comprise 9 or 10 months instead of 12 months.

STUDY OUTCOMES

The study has three main outcome measures. First, the percentage of STEMI patients in which the PCI procedure started within 90 minutes from first (para)medical contact. Second, the percentage of NSTEMI or UA patients where use of a validated risk scoring instrument was documented. Finally, the percentage of ACS patients with a prescription

of the recommended discharge medication, documentation of a contraindication or other reason for not receiving the recommended medication. Additionally, patient and hospital characteristics associated with guideline adherence will be identified.

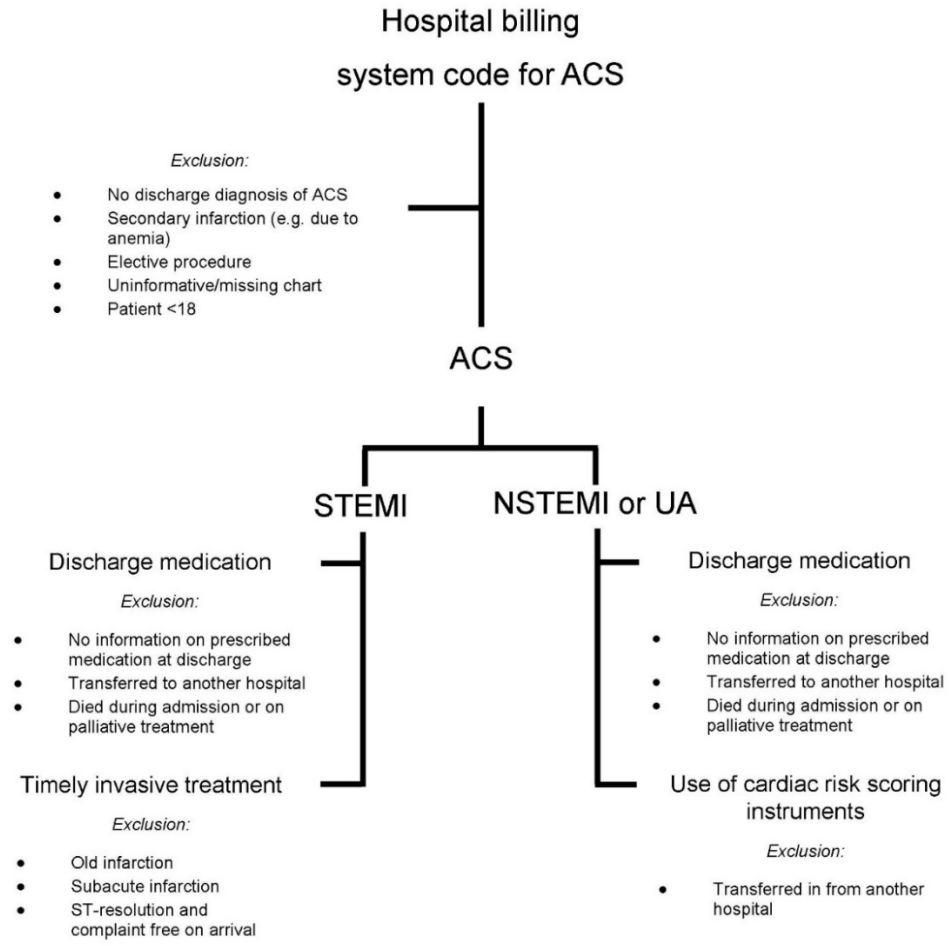

Figure 1. Flow chart of the selection of patient charts. *ACS* acute coronary syndrome; *STEMI* ST-segment elevation myocardial infarction; *NSTEMI* non-ST-segment elevation myocardial infarction; *UA* unstable angina

Table 2. Information recorded for all ACS patients

General information
- Gender
- Date of birth
- Admission date and time
- Complaints
- Discharge date
- Discharge status (discharged, deceased, unknown)

History of cardiac disease (yes/no)
- Coronary vascular disease
- Peripheral vascular disease
- (Unstable) angina pectoris
- Acute myocardial infarction
- Coronary artery bypass graft surgery, year: _____
- Percutaneous coronary intervention, year: _____
- Intervention/acute myocardial infarction < 6 months

Risk factors (yes/no)
- Diabetes mellitus
- Hypertension
- Kidney failure
- Chronic heart failure
- Positive family history
- Smoker
- Previous smoker
- Elevated cholesterol levels (statin use in history, hyperlipidaemia, hypercholesterolemia)
- Obesity (body mass index >30 kg/m2)
- Obesity (body mass index >30 kg/m2)
- Coronary stenosis >50% (in history)
- Age >70 year
- Male sex
- Aspirin use (<7 days)

Vital functions
- Cardiogenic shock (yes/no)
- Heart failure (yes/no)
- Resuscitation (yes/no)
- Blood pressure on arrival
- Heart rate (beats per minute)
- Electrocardiogram date and time
- Electrocardiogram interpretation
- Biomarker values (troponin, creatinin kinase (CK), creatinin kinase-muscle/brain (CK-MB), creatinin)

Discharge medication (yes/no)
- Acetylsalicylic acid
- Thienopyridine
- Statin
- Beta blocker
- Angiotensin Converting Enzyme-inhibitor

Contraindications (yes/no)

Acetylsalicylic acid
- Coagulation defect
- Active peptic ulcer (ulcus pepticum)
- Stroke (bleeding)
- Liver failure
- Kidney failure
- Allergy/oversensitivity
- Treatment with anti-coagulant medication
- G6PD-deficiency
- Other:

Thienopyridine
- Transient ischemic attack/cerebrovascular accident
- Active peptic ulcer (ulcus pepticum)
- Liver failure
- Pathological bleeding (from ulcus pepticum or intracranial bleeding)
- Other:

Statin
- Liver function impairment
- Renal impairment
- Other:

Beta blocker
- Sick-sinus syndrome
- 2nd and 3rd degree AV-block (ECG)
- Hypotension
- Cardiogenic shock
- Sinus bradycardia
- Unstable or untreated heart failure
- Pheochromocytoma
- Bronchial asthma (anamnesis)
- Severe peripheral circulation defects
- Metabolic acidosis
- Pulmonary hypertension
- Kidney failure
- Liver failure
- Myocardial infarction with heart frequency <45, P-Q >0.24, systolic blood pressure <100

Cardiac rehabilitation (yes/no)	Other:
Enlistment for cardiac rehabilitation	*Angiotensin Converting Enzyme-inhibitor*
	Kidney failure
	Other

ACS = Acute Coronary Syndrome

RECORDED VARIABLES

From all charts, the following information is abstracted: demographic and clinical information including gender, age, cardiac history, risk factors, biomarker values, electrocardiogram findings, resuscitation, heart failure, cardiogenic shock on arrival and month of discharge (Table 2).

In addition, for the timely invasive treatment indicator, the following variables are recorded: routing of the patient, type of first (para)medical contact, place of first electrocardiogram, type of treatment, and the dates and times of first (para)medical contact, first (ambulance/general practitioner) electrocardiogram and sheath insertion (start of PCI) (Table 3).

Table 3. Additional recorded variables for STEMI patients

General information
Routing out-of-hospital
Type of treatment (pharmacological, acute percutaneous coronary intervention, non-acute percutaneous coronary intervention, coronary artery bypass graft surgery)
Discipline of first (para)medical contact
Discipline of first electrocardiogram
Number of diseased vessels
Location of stenoses
Time variables
Symptom onset
First (para)medical contact
First electrocardiogram
Sheath insertion
First balloon inflation or thrombus aspiration

STEMI = ST-segment Elevation Myocardial Infarction

To evaluate cardiac risk score adherence, application of a validated risk scoring instrument (e.g. GRACE[18, 19], TIMI[20], FRISC[21], HEART[22] and PURSUIT[8]), type of instrument, risk score outcome, date of application, and type of treatment are recorded (Table 4).

Table 4. Additional recorded variables for NSTEMI and UA patients
General information
Routing in-hospital
Catheterization (yes/no)
Type of treatment (pharmacological, percutaneous coronary intervention, coronary artery bypass graft, unknown, other)
Risk score
Use of validated risk score (yes/no)
Date of application
Type of instrument(s)
Risk score outcome
Risk score outcome classification
Additional diagnostics

NSTEMI = Non-ST-segment Elevation Myocardial Infarction; UA = Unstable Angina

Finally, for discharge medication, prescription of acetylsalicylic acid, thienopyridine, statin, beta blocker and angiotensin-converting enzyme (ACE) inhibitor and contraindications or other reasons for not prescribing all or some of the medication are recorded (Table 2). Contraindications were derived from an annually updated database containing information about all medication registered in the Netherlands.[23]

ABSTRACTION OF DATA

All data are collected on standard case report forms. Variables are defined in codebooks. Two researchers (JT & JE) developed the codebooks and case report forms based on the European Society of Cardiology guidelines. The case report forms were discussed within the research group, tested in two pilot measurements and adjusted accordingly. The data are collected by six chart abstractors who were introduced to the subject of ACS and instructed in the chart review procedures by JT and JE. Chart reviews were supervised until the quality of the chart reviews was satisfactory. The data are entered into a database using a data entry program with fixed entry fields (BLAISE version 4.7, Statistics Netherlands) and compared with the original case report form by a second researcher.

To ensure reliability of the data and to assess the quality of the codebook, a sample of charts (5–10 %) is independently screened again by one of the five other chart abstractors. The two case report forms are compared, and differences are discussed until consensus is reached. If necessary, changes are made in the original case report form. The reliability between the chart abstractors will be calculated by means of the percentage of agreement for each variable.

STATISTICAL ANALYSES

MISSING DATA

Missing data patterns will be analysed by means of missing value analyses. Depending on the pattern[24], missing values will be imputed by means of a single imputation (missing completely at random) or multiple imputation procedure (missing at random)[25].

DESCRIPTIVE STATISTICS

The degree of adherence to the three process indicators will be presented by descriptive statistics. Associations of patient and hospital characteristics with guideline adherence are studied in separate analyses.

TIMELY INVASIVE TREATMENT

The time to PCI in minutes will be entered as a continuous dependent variable in a generalised linear model taking into account its distribution, as time variables are generally not normally distributed. In univariate analyses, associations of the independent variables, i.e. patient and admission characteristics, are studied. To account for clustering of patient data within hospitals, the variable 'hospital' and its significant interactions with any other of the predictor variables will be entered as a covariate in all univariate models.[26] This is because the hospital sample size (7 PCI-capable hospitals) is considered small for multilevel regression analysis.[27] All variables and interactions significantly ($p \leq 0.05$) associated with the time to PCI will be included in the multiple generalised linear model. Furthermore, to minimise the probability of making a type II error, all non-significant variables from the univariate models will be added to the multiple generalised linear model one by one. Significant variables ($p \leq 0.05$) will be added to the final model.

USE OF RISK SCORING INSTRUMENTS

Associations of independent variables with the use of cardiac risk scoring instruments will be studied by means of a generalised linear mixed model (GLMM). In the analysis, the binary dependent variable will be the use of a validated risk score instrument. Independent variables will be patient characteristics, hospital characteristics and month of discharge. To account for clustering of the data, the model will comprise random effects for hospitals. First, independent variables will be tested separately correcting for the random hospital effects. Second, all independent variables with a significance level below $p \leq 0.15$ will be selected. Next, pairs of selected independent variables will be tested jointly.

Last, all significant ($p \leq 0.05$) variables from the previous steps will be included in the final multivariable model. This final step also comprises a cautious consideration of significant ($p \leq 0.05$) interaction terms.

DISCHARGE MEDICATION

Associations of independent variables with the prescription of the recommended discharge medication will be studied by means of GLMM. In these analyses, prescription of the five guideline-recommended medicines or documentation of contraindications (yes/no) will be the binary dependent variable. The effects of the independent variables including patient, hospital and discharge characteristics will be tested in univariate analyses. All variables with a significant association ($p \leq 0.05$) with the dependent variable will be included in a multivariable model. To account for the effects of collinearity, all variables not significantly related to prescription of the recommended discharge medication in the univariate models will be added to the multivariable generalised linear mixed model one by one. Interactions will be tested and added to the multivariable model in case of a significant effect. In all models, hospital will be entered as a random effect variable to account for clustering of the data. As not all medicines are indicated for all patients with ACS according to the European Society of Cardiology guidelines (e.g. ACE-inhibitors are recommended for all patients with ACS, but only indicated for those patients with a reduced cardiac function), additional models will be created to analyse the effects of patient and hospital characteristics on the prescription of ≤3 and ≥4 medicines or documentation of a contraindication.

SOFTWARE

The data will be analysed in IBM SPSS Statistics (version 20 for Windows) and R (version 3.0.0 for Windows).

ETHICAL APPROVAL AND CONFIDENTIALITY

The study protocol was approved by the medical ethics review committee of the VU University Medical Centre. To protect patients' and hospitals' privacy, they are assigned a unique observation code. All data are stored on a password protected network server of the VU University Medical Centre, to which only the participating researchers have access. All chart abstractors signed a confidentiality agreement and the study was registered with the Dutch Data Protection Agency.

DISCUSSION

This paper describes the design of a study of the quality of Dutch ACS care by evaluating the degree to which hospitals adhere to three key quality indicators from (inter)national guidelines and by exploring factors associated with guideline adherence.

Previous North American studies that monitored guideline adherence have successfully identified associated factors[10, 16, 28], after which targeted quality improvement efforts could be applied. These efforts increased the likelihood that patients were treated on time with PCI[29], risk scores were documented [30] and the recommended discharge medication was prescribed[31]. Therefore, the monitoring of guideline adherence as the foundation for targeted quality improvement efforts seems promising.

The three guideline recommendations evaluated in this study were selected from the European Society of Cardiology guidelines[12, 13], but are also included in other (inter) national guidelines[32-34]. The methods used in this study can be applied to evaluate the process of ACS care in other countries, especially in countries where large, national registries of guideline adherence are lacking.

POTENTIAL LIMITATIONS

In designing the study, several limitations have to be taken into account. First, the documented information in the charts and variability between the chart abstractors may affect the reliability of the data. This will be reduced by using standardised case report forms, a codebook and by interim reliability checks of the data. Second, using the diagnosis in the discharge letter as inclusion criterion may not be as reliable as applying our own diagnostic criteria. However, it was considered important to take into account the interpretation of the treating physician at the time of hospitalisation of the patient. Third, the presence of researchers on site, and quarterly feedback from the national quality improvement program might influence hospitals' performance on the outcomes. However, in a report on the evaluation of the quality improvement program the effect of this national intervention was limited[35]. Finally, the selection of hospitals and patients could not be performed completely randomly due to practical limitations. However, the hospitals included in this study were geographically spread over the country, thereby limiting the influence of potential regional variation in guideline adherence. Additionally, the outcomes of this study are corrected for the influence of individual hospitals in the statistical models.

CONCLUSION

Evidence-based guidelines are of vital importance in safely and effectively treating patients diagnosed with ACS. The results of this study will provide insight into the degree of guideline adherence in Dutch hospitals for the management of patients with ACS and identify room for further improvement. Furthermore, patient and hospital characteristics associated with guideline adherence will be identified, which may facilitate targeted improvement strategies.

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CONFLICT OF INTEREST

None declared.

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Chapter 3

Exploring the treatment delay in the care of patients with ST-elevation myocardial infarction undergoing acute percutaneous coronary intervention: a cross-sectional study

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ABSTRACT

Background: A short delay between diagnosis and treatment for patients diagnosed with ST-elevation myocardial infarction (STEMI) is vital to prevent cardiac damage and mortality. The objective of this study was to explore the treatment delay and associated factors in the management of patients diagnosed with STEMI going for percutaneous coronary intervention (PCI).

Methods: In a cross-sectional multicentre study, the treatment delay (time between first electrocardiogram and start of PCI procedure) of STEMI patients in seven PCI centres in the Netherlands was measured. Data were analyzed by means of multivariable generalized linear models, accounting for a non-normally distributed outcome and clustering of patients within centres.

Results: In total, 1017 patient charts were included. The majority of the patients (78.7 %) were treated within the guideline recommended time target of 90 min. Overall, the median treatment delay was 64 min (interquartile range 47–82). A significantly prolonged delay was found among patients of whom their first electrocardiogram was performed at a general practitioner's practice (+23.9 min; 95 % confidence interval 9.9–40.8) or in-hospital (+9.5 min; 95 % confidence interval 2.5–17.3), patients requiring interhospital transfer (+14.6 min; 95 % confidence interval 7.6–22.4) or presenting with acute heart failure on admission (+17.6 min; 95 % confidence interval 7.9–28.7).

Conclusions: Despite a short median delay between first electrocardiogram and PCI, the time targets are occasionally exceeded for patients diagnosed with STEMI. To further improve the process of care, PCI centres should focus on improving regional STEMI care networks, involving general practitioners, emergency departments and referring hospitals.

BACKGROUND

There is a strong association between the time to reperfusion treatment and mortality for patients with ST-elevation myocardial infarction (STEMI).[1] Every 30 min delay from symptom onset to percutaneous coronary intervention (PCI) increases patients' risk of dying by 7.5 %.[2] In contrast to other factors that influence the likelihood of dying from STEMI, e.g. heart failure, diabetes or an anterior infarction,[3] the time to PCI can be influenced immediately by health care providers. Furthermore, time to PCI can be reduced in the long run by optimizing the process of care within PCI centres and regions.[4]

The importance of timely PCI treatment has been acknowledged by the European Society of Cardiology in their guidelines on the management of patients diagnosed with STEMI.[5] These guidelines recommend primary PCI over fibrinolysis as the preferred reperfusion treatment, yet only when it can be performed within 120 min after first (para) medical contact. However, treatment within 90 min from first (para) medical contact is highly preferred, or even within 60 min in case the patients' symptoms started less than two hours ago, or they present directly to a PCI centre.

Despite these recommendations, previous studies reported that a substantial number of patients are not treated within the recommended time targets, putting them at increased risk of dying from STEMI.[6-8] Certain patient groups experienced a longer treatment delay e.g. patients who are transported from a referring hospital to a PCI centre (interhospital transfer).[9,10] Since these studies were performed, new management guidelines for STEMI were published by the European Society of Cardiology which recommend strategies on limiting delay, e.g. by building STEMI care networks consisting of PCI centres, referring hospitals and ambulance services.[5]

In the Netherlands, 30 out of 91 hospitals provide PCI, serving an average population of approximately 0.6 million citizens per PCI centre. Due to the good geographical accessibility of PCI centres in the Netherlands,[11] PCI is the standard treatment for all patients diagnosed with STEMI without contra-indications for PCI. Once patients contact the ambulance services and they are suspected of STEMI, the goal is to directly transport them to the nearest PCI centre.[12] However, patients can also contact the general practitioner or emergency department, resulting in deviating patient routes.

The process of care for patients with STEMI going for PCI is complex, and improving it is difficult.[13] By identifying patients with a prolonged treatment delay, improvements in the current strategies can be facilitated or additional strategies can be developed. In the present study, the degree to which patients were treated within the European guideline recommended time targets was explored, as well as patient and admission characteristics associated with a prolonged treatment delay.

METHODS

STUDY DESIGN

A cross-sectional multicentre study was conducted in the Netherlands. The study design, setting and methods have been previously described in detail elsewhere[14] and are briefly outlined below.

SETTING AND POPULATION

In total, seven PCI centres in the Netherlands, selected by means of a multistage random selection procedure, participated in the present study. The number of acute PCI procedures for STEMI patients performed by the included PCI centres ranged from approximately 250 to more than 500 procedures per year, and five centres also provided thoracic surgery (Table 1).

Table 1. PCI centre characteristics (n=7)

Centre nr	Type	Thoracic surgery	Nr of acute PCIs for STEMI per year*	Nr of patients included
1	Teaching	No	<300	127
2	Teaching	Yes	>500	112
3	Teaching	No	300-400	171
4	Academic	Yes	>500	236
5	Academic	Yes	400-500	139
6	Teaching	Yes	>500	112
7	Teaching	Yes	400-500	120

* Based on data from the Dutch health care inspectorate, categorized to guarantee anonymity of the participating centres

PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction

Monthly, from each PCI centre patients diagnosed with STEMI who were discharged between January 1stand December 31st of 2012 were preselected by means of the hospital financial system codes. The charts were screened manually to confirm a documented discharge diagnosis of STEMI. In case the discharge diagnosis was unclear or ambiguous, the chart was discussed with a cardiologist or other on-site physician working in cardiology. Charts of patients without a discharge diagnosis of STEMI, a secondary infarction (e.g. due to anaemia) or with insufficient information were excluded from the study. Also, charts of patients with a documented sub-acute or old infarction (e.g. patients with an infarction of more than 12 h old, where PCI offers no clinical benefit over pharmacological treatment anymore), or ST-resolution on the electrocardiogram in combination with the absence of symptoms on admission were excluded from the study. Finally, charts of patients with a treatment delay of more than 6 h were excluded

from the study, as it was unlikely that the goal was to treat these patients with PCI immediately. As a result of the eight hour shifts of the data abstractors, patients were included in the study in chronological order of discharge until the researchers were practically unable to screen additional charts on the day of the measurement.

DATA COLLECTION

Data were abstracted from patient charts by six researchers. Because the time of first (para) medical contact was not registered consistently in all PCI centres, the time of the first (pre) hospital electrocardiogram was abstracted. In case patients developed a STEMI while being hospitalized for another illness or complaint, the time of the first electrocardiogram with ST-elevation in-hospital was registered. In addition, the time of sheath insertion at the catheterization room was registered as start of the PCI procedure. As a result, the treatment delay was defined as the time between first (diagnostic) electrocardiogram and sheath insertion. Additionally, demographic characteristics, cardiac risk factors, cardiac history and admission characteristics were abstracted from patient charts.

To ensure reliable data abstraction 80 charts (6.8 %) were screened by two researchers independently and the findings were compared. Differences were discussed until consensus was reached and adapted in the original case report form accordingly. Interrater reliability was calculated by means of percentages agreement for each extracted variable and ranged between acceptable (70 %) and perfect (100 %), with exception of the variable 'type of first (para) medical contact' (68 %). As a result of the latter variable's lower reliability and its unlikely influence on the delay starting from first electrocardiogram, this variable was excluded from the analyses.

MISSING DATA

The treatment delay was calculated by determining the difference in minutes between the first electrocardiogram and sheath insertion. The resulting values were screened and negative values were set to missing.

In total, 6.8 % of the values of all variables in the dataset were missing. The percentage of missing values per variable ranged from 0.1 % (i.e. resuscitation, age, length of stay) to 31.6 % (time from chest pain to first electrocardiogram). The variables gender, month of discharge and weekend presentation had no missing values. To explore the underlying missing data mechanism, associations between missing and non-missing values were studied and Little's test was conducted in IBM SPSS (version 20 for

Windows). The test was significant ($p < 0.001$), indicating that missing values in the dataset were not missing completely at random but either missing at random or missing not at random.[15] As a result, the missing data were imputed with multiple imputation by assuming the data were missing at random, in which the probability for a variable being missing is dependent on the value of other variables in the dataset. The data were imputed following the approach of van Buuren.[16] Prior to imputation, non-normally distributed continuous variables i.e. time from chest pain to electrocardiogram, treatment delay, and creatinine level on admission were transformed using the Box-Cox power transformation.[17] In total, 32 imputed datasets were created, following recommendations of White *et al.*.[18] The plausibility of the imputed data and the assumed missing data mechanism were checked by exploring the distributions of the imputed data in comparison to the original data. In these analyses, it appeared that the distributions of the imputed variables were comparable to those of the original data. It was therefore assumed that the imputation resulted in plausible values. After imputation, all transformed variables were transformed back to their original units. Model estimates were calculated for each dataset and pooled using Rubin's rules embedded in the *mice* procedure.

Data were imputed using the *mice* package in R (version 3.0.0 for Microsoft Windows).[19]

STATISTICAL ANALYSES

Descriptive statistics were used to report patient and admission characteristics as well as to determine the frequency of patients who were treated within 90 and 120 min after first electrocardiogram. In addition, we investigated the frequency of being treated within 60 min for the subgroup of patients whose symptoms started less than 2 h ago or who presented directly to a PCI centre. For continuous variables with an approximately normal distribution, the means with 95 % confidence intervals (CI) are described, while for continuous variables with a skewed distribution the medians with interquartile ranges (IQR) are described. The associations of patient and admission characteristics with the treatment delay were tested using generalized linear models which take into account a skewed (Gamma distributed) outcome variable. Additionally, a log link was applied because negative time values are impossible.

The goal of the study was to explore factors associated with the treatment delay. Therefore, in univariate analyses, it was tested which variables were significantly ($p < 0.05$) associated with treatment delay. Explanatory variables with a significant

effect on treatment delay were entered into a multivariable generalized linear model. To correct for clustering of patients in PCI centres, the variable 'PCI centre' was added as a covariate in all analyses. Moreover, the process of care might differ between PCI centres, and therefore associations between explanatory variables and the outcome variable might differ. To correct for these differences, interaction terms between the explanatory variables and PCI centre were tested and added to the model in case they significantly improved the model fit.

Additionally, because collinearity can lead to unjustified exclusion of explanatory variables, all variables not significantly associated in the univariate analyses were added to the multivariable model one by one. Variables with a significant improvement of the model fit were added to the final multivariable model. The results of the final multivariable model were interpreted as the minimal delay in minutes per variable, holding all other variables constant. As a result of the underlying missing data pattern of missing at random, all reported results were based on analyses of the imputed data.

ETHICAL APPROVAL

The study protocol was approved by the medical ethical review committee of the VU University medical centre. Anonymity of patients and PCI centres was protected by coding patient and centre characteristics i.e. no names or addresses of patients or centres, or patient identification numbers were recorded. Data were stored on a password protected network of the EMGO+ / VU University medical centre. All chart abstractors signed confidentiality agreements, and the study was registered with the Dutch Data Protection Agency.

RESULTS

In total, a sample of 1170 charts of patients with a confirmed discharge diagnosis of STEMI was selected. Of these charts, 150 (12.8 %) patients received pharmacological treatment or non-acute PCI, and 3 (0.3 %) had a treatment delay of more than six hours. These patient charts were subsequently excluded from the study, leaving 1017 charts for further analyses. The number of included charts per PCI centre ranged from 112 to 236.

The mean age of patients presenting with STEMI and going for acute PCI was 62.5 years (95 % confidence interval: 61.3–63.7) (Table 3). The median time between symptom onset and first electrocardiogram was 81 min (interquartile range: 20–142) (Table 4).

TREATMENT WITHIN GUIDELINE RECOMMENDED TIMES

The treatment times and ischemic times of the observed data are presented in Table 2. After imputation of the missing values, the median time from first electrocardiogram to PCI was 64 min (interquartile range: 47–82). PCI centres were able to treat 800 (78.7 %) patients within 90 min from first electrocardiogram with PCI, and 918 (90.3 %) patients within 120 min. Of the patients who presented within two hours of symptom onset or who presented directly to a PCI centre ($n = 700$), 312 (44.6 %) were treated within 60 min as recommended by the guidelines.

FACTORS ASSOCIATED WITH TREATMENT DELAY

In univariate analyses, of the patient characteristics, a prior myocardial infarction ($p = 0.046$) and prior use of anticoagulants (within the last seven days) ($p = 0.007$) were significantly associated with treatment delay (Table 3).

Moreover, of the admission characteristics, the location where the first electrocardiogram was made ($p < 0.001$), interhospital transfer for PCI ($p < 0.001$), acute heart failure on admission ($p < 0.001$), creatinine level on admission ($p = 0.03$) and a stenosis in the left anterior descending coronary artery ($p = 0.03$) were significantly associated with treatment delay (Table 4).

When looking at differences in delaying factors per PCI centre, no interactions of PCI centre with patient or admission characteristics were significantly associated with treatment delay.

Variables with a significant association with treatment delay in univariate models were added to a multivariable generalized linear model. One variable with a non-significant association in univariate analyses improved the multivariable model fit (stenosis in the circumflex artery, $p = 0.03$) and was added to the multivariable model. No interactions significantly improved the multivariable model fit. In the final multivariable model, patients of whom their first electrocardiogram was performed at a general practitioner (+23.9 min; 95 % CI 9.9–40.8) or hospital (+9.5 min; 95 % CI 2.5–17.3) had an additional treatment delay compared to patients of whom their first electrocardiogram was made in the ambulance (Table 5). Moreover, patients who required interhospital transfer (+14.6 min; 95 % CI 7.6–22.4), with acute heart failure on admission (+17.6 min; 95 % CI 7.9–28.7) or with a stenosis in the circumflex artery (+4.3 min; 95 % CI 0.4–8.6) had a significantly longer treatment delay.

Table 2. Treatment delay and ischemic time in various patient groups based on observed data

Characteristic	n	missing (%)	treatment delay*	missing (%)	ischemic time**
All patients	1017	139 (13.7%)	64 (51-84)	330 (32.4%)	148 (105-266)
Interhospital transfer for PCI	1009				
- yes	199	25 (21.6%)	77 (58-110)	76 (38.2%)	173 (118-274)
- no	810	110 (13.6%)	62.0 (49-79)	248 (30.6%)	145 (101-219)
First ECG	874				
- General practitioner	25	2 (8.0%)	86 (68-113)	4 (16.0%)	199 (161-341)
- Ambulance	707	55 (7.8%)	62 (49-78)	184 (26.0%)	141 (100-215)
- Hospital	142	10 (7.0%)	77 (60-111)	49 (34.5%)	189 (119-324)

* Treatment delay was defined in minutes as ranging from first electrocardiogram with ST-elevation to start of the percutaneous coronary intervention and is not corrected for the effects of other independent variables
** Ischemic time was defined in minutes as ranging from symptom onset to start of the percutaneous coronary intervention
PCI = percutaneous coronary intervention; ECG = electrocardiogram

Table 3. Original and imputed admission characteristics and associations with on treatment delay in univariate analysis (n=1017)

Variable	missing (%)	value	imputed value	p-value*
Time from chest pain to ECG (median (IQR) minutes)	321 (31.6%)	78 (41-148)	81 (20-142)	0.12
Treatment delay (median (IQR) minutes from ECG to PCI)	139 (13.7%)	64 (51-84)	64 (47-82)	N/A
First ECG	143 (14.1%)			**<0.001**
- General practitioner		25 (2.9%)	34 (3.3%)	
- Ambulance		707 (80.9%)	809 (79.6%)	
- Hospital		142 (16.2%)	174 (17.1%)	
Weekend presentation	0 (0%)	291 (28.6%)	291 (28.6%)	0.92
Weekday evening presentation	152 (14.9%)	385 (44.5%)	450 (44.2%)	0.15
Month of discharge	0 (0%)	N/A	N/A	0.72
Interhospital transfer for PCI	8 (0.8%)	199 (19.7%)	200 (19.7%)	**<0.001**
Systolic blood pressure on admission (mean (SD) mmHg)	45 (4.4%)	130 (26)	130 (27)	0.82
Heart rate on admission (mean (SD) beats/minute)	161 (15.8%)	75 (18)	75 (18)	0.48
Resuscitation	1 (0.1%)	99 (9.7%)	99 (9.7%)	0.31
Acute heart failure on admission	54 (5.3%)	47 (4.9%)	58 (5.7%)	**<0.001**
Cardiogenic shock on admission	71 (7.0%)	37 (3.9%)	46 (4.5%)	0.06
Creatinine level on admission (median (IQR) mmol/L)	112 (11.0%)	78 (66-91)	77.8 (65.0-90.6)	**0.03**

Table 3 continued. Original and imputed admission characteristics and associations with on treatment delay in univariate analysis (n=1017)

Variable	missing (%)	value	imputed value	p-value*
Nr of diseased vessels	22 (2.2%)			0.56
- One		555 (55.8%)	566 (55.7%)	
- Two		264 (26.5%)	269 (26.4%)	
- Three		176 (17.7%)	182 (17.9%)	
Location stenoses †				
- Left main	7 (0.7%)	27 (2.7%)	27 (2.7%)	0.20
- Right coronary	6 (0.6%)	565 (55.9%)	569 (55.9%)	0.10
- Left anterior descending	5 (0.5%)	648 (64.0%)	652 (64.1%)	**0.03**
- Circumflex	7 (0.7%)	400 (39.6%)	405 (39.8%)	0.06

* P-values are calculated using the Wald statistics, comparing a generalized linear model with and without the imputed variable, corrected for clustering of patients in PCI centres
† Only stenoses ≥50%. A single patient can have more than 1 stenosis
ECG = electrocardiogram; IQR = interquartile range; PCI = percutaneous coronary intervention; N/A = not applicable; SD = standard deviation; mmHg = millimeter of mercury; mmol/L = millimoles per litre
Significant results are highlighted in **bold**

Table 4. Associations of patient characteristics with time from first electrocardiogram to PCI in the multivariable analysis

Variable	% increase in treatment delay (95% CI)		Minimal increase in treatment delay in minutes (95% CI)*		p-value
Intercept	N/A		59.8	(51.5;69.4)	N/A
Prior myocardial infarction	3.0%	(-7.6;14.9)	1.8	(-4.5;8.9)	0.59
Prior use of anticoagulants (≤7 days)	6.7%	(-2.3;16.5)	4.0	(-1.4;9.9)	0.15
First ECG at the general practitioner	40.0%	(16.5;68.2)	23.9	(9.9;40.8)	**<0.001**
First ECG in the hospital	15.9%	(4.1;28.9)	9.5	(2.5;17.3)	**0.007**
Interhospital transfer for PCI	24.4%	(12.7;37.4)	14.6	(7.6;22.4)	**<0.001**
Acute heart failure on admission	29.5%	(13.2;48.0)	17.6	(7.9;28.7)	**<0.001**
Creatinine level on admission (per mmol/L)	0.1%	(-0.04;0.2)	0.06	(-0.02 ;0.14)	0.16
Stenosis in left anterior descending	4.1%	(-2.2;10.9)	2.5	(-1.3;6.5)	0.21
Stenosis in circumflex artery	7.3%	(0.6;14.4)	4.3	(0.4;8.6)	**0.03**

N/A = not applicable; CI = confidence interval; PCI = percutaneous coronary intervention; ECG = electrocardiogram
Significant results are highlighted in **bold**
* As a result of the generalized linear model with a gamma distributed outcome and a log link, combining the effects of independent variables should be performed with caution due to multiplicative (and not additive) effects

DISCUSSION

Treating STEMI patients with primary PCI within the guideline recommended time frames is complex, and strategies to achieve them have been published in international guidelines in recent years. In this study, the treatment delay of patients with STEMI and associated factors were explored. Despite a median treatment delay of 64 min, the time target of 90 min was exceeded in 21.3 % of the patients. In an attempt to explain these findings, factors associated with a prolonged treatment delay were identified. Patients of whom an electrocardiogram was made at a general practitioner or hospital, patients requiring interhospital transfer for PCI, patients with acute heart failure or with a stenosis in the circumflex artery were more likely to experience a prolonged treatment delay. These patients have an increased but potentially preventable risk of cardiac damage and dying.

Several studies have investigated treatment delay previously, and found a longer median treatment delay than in this study.[9, 10, 20] This finding may be explained by the use of a different definition of delay, e.g. from first (para) medical contact to PCI instead of first electrocardiogram to PCI. It may also be explained by the relatively high number of PCI centres in the Netherlands distributed over the country, resulting in good geographical accessibility.

The delaying factors identified in this study are comparable to other studies, in which patients who were transferred between hospitals had a prolonged treatment delay.[9, 10, 21] Also, a prolonged treatment delay and higher mortality were found for patients who first contacted a general practitioner instead of direct contact with emergency medical services or the hospital.[22] However, in the present study, patients of whom their first electrocardiogram was made at a hospital also had a prolonged delay than patients who contacted the emergency medical services directly. These findings confirm that contacting the ambulance services when experiencing cardiac complaints is of vital importance for patients with a potential STEMI in limiting treatment delay. While transporting a patient directly to a PCI centre, ambulance services can contact the PCI centre and initiate catheterization room activation.[23] This supports the European Society of Cardiology recommendation that the general population should be encouraged to contact the ambulance services instead of the general practitioner or hospital when experiencing symptoms of STEMI.[5] However, influencing the behaviour of potential STEMI patients is difficult.[24, 25] Therefore, new interventions to reduce patient delay are required, but until then improvement efforts should focus on reducing system delay (time from first (para) medical contact to wire passage).

Additionally, there has been a call to form STEMI care networks with which providers of STEMI care can initiate interventions to speed up the process of care. In the Netherlands, this initiative has resulted in a national program to improve organization of STEMI care per region.[26] For these initiatives, it is recommended to involve all relevant stakeholders i.e. PCI centres, referring hospitals, emergency departments and general practitioners within the network region. Previous improvement studies which excluded patients who were transferred between hospitals found no significant survival benefit of reducing the door-to-balloon time by 16 min.[27] In this study, we have shown that interhospital transfer was one of the strongest predictor for a prolonged treatment delay. These patients therefore potentially benefit the most from reducing the treatment delay, which might result in improvements in survival. Consequently, in future studies it is important to include all patients undergoing primary PCI.

The finding that patients with acute heart failure were more likely to experience a prolonged treatment delay than patients without acute heart failure may be explained by the fact that they require more elaborate stabilization in the acute care phase. It is uncertain whether this delay can be reduced without compromising the safety of the patient, and therefore a longer delay might have to be accepted.

Also, patients presenting with a stenosis in the circumflex artery experienced a significantly prolonged treatment delay. A stenosis in the circumflex artery might indicate a lateral or posterior infarction. These patients tend to present with limited electrocardiogram abnormalities,[28] which hampers rapid diagnosis. Use of a posterior electrocardiogram in the ambulance may speed up diagnosis and reduce the treatment delay for these patients. However, the difficulty of interpreting a posterior electrocardiogram might result in unnecessary activations of the catheterization room, and continuous education for paramedics in the regional STEMI care networks might be required.

LIMITATIONS

Some limitations of this study need to be taken into account when interpreting the results. First, the time from first (para) medical contact to wire passage, as specified in the European Society of Cardiology guidelines, was not registered in all participating PCI centres. Therefore, the time from first electrocardiogram (diagnosis) to sheath insertion was used to determine the treatment delay. This definition is only part of the time to reperfusion as described in cardiac guidelines,[5, 6] who differentiate between

patient delay (symptom onset to first (para) medical contact) and system delay (first (para) medical contact to wire passage). As a consequence, the results of this study underestimate the treatment delay of STEMI patients in the Netherlands compared to other studies.[29]

Second, the treatment times registered in the participating PCI centres were not primarily registered for scientific research. This could potentially compromise the validity of the registered times, which would have affected the reliability of the study findings. However, we used automatically registered times as much as possible, i.e. times registered on an electrocardiogram or in the catheterization room system, and checked the plausibility of the calculated treatment delay. Also, the equivalent time variables were used by PCI centres to report quality indicators to the national government and were therefore also used to make policy decisions.

Third, the PCI centre in which a patient was treated was only used as a statistical correction in this study because of size differences between the regions in which centres were located. Consequently, in case of significant differences in the treatment delay between centres, it would be impossible to differentiate between differences caused by regional size or by differences in health care organization.

Fourth, in this study it was not possible to identify the correlation between treatment delay and hospital mortality. In the Netherlands, it is common practice to transport the patient from the PCI centre to their local hospital shortly after the PCI procedure for follow-up care. Due to Dutch privacy regulations, no information of patients could be linked for research purposes between hospitals. As a result, no information about hospital mortality could be obtained.

Finally, chart review is a data collection method with a high risk of missing values. However, it would be inappropriate to delete all cases with missing values as this can introduce bias in the study population. Therefore, extensive methods were used in this study to account for these missing values.

CONCLUSIONS

Despite a median treatment delay within guideline recommendations, patients diagnosed with STEMI who required PCI treatment were occasionally not treated on time as recommended in the European guidelines. A first electrocardiogram made at the general practitioner or hospital, and interhospital transfer resulted in a prolonged treatment delay for these patients. To further improve the process of care, efforts should focus on strengthening STEMI care networks, incorporating all relevant stakeholders in a region including general practitioners, referring hospitals and emergency departments.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

JT, MdB and CW designed the study. JT collected the data, performed the statistical analyses and drafted the manuscript. IvdW provided supervision, assisted in the statistical analyses and helped to draft the manuscript. MdB and CW revised subsequent versions of the manuscript. All authors read and approved the final manuscript.

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Chapter 4

Data quality issues impede comparability of hospital treatment delay performance indicators

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ABSTRACT

Aim: To assess the comparability of five performance indicator scores for treatment delay among patients diagnosed with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention in relation to the quality of the underlying data.

Methods: Secondary analyses were performed on data from 1017 patients in seven Dutch hospitals. Data were collected using standardised forms for patients discharged in 2012. Comparability was assessed as the number of occasions the indicator threshold was reached for each hospital.

Results: Hospitals recorded different time points based on different interpretations of the definitions. This led to substantial differences in indicator scores, ranging from 57 to 100% of the indictor threshold being reached. Some hospitals recorded all the required data elements for calculating the performance indicators but none of the data elements could be retrieved in a fully automated way. Moreover, recording accessibility and completeness of time points varied widely within and between hospitals.

Conclusion: Hospitals use different definitions for treatment delay and vary greatly in the extent to which the necessary data are available, accessible and complete, impeding comparability between hospitals. Indicator developers, users and hospitals providing data should be aware of these issues and aim to improve data quality in order to facilitate comparability of performance indicators.

INTRODUCTION

Assessment of the quality of care by means of performance indicators is an integral part of modern day health care. Performance indicators are a tool in quality improvement and provide the government, physicians, patients, scientific society and insurance companies an indication of hospital performance, which is increasingly demanded.[3] As comparing performance indicator scores between hospitals can have major consequences, including lay press ranking lists and government and insurance company sanctions, performance indicator scores need to be comparable.

There are several steps in the process that leads from an event happening in clinical practice to a performance indicator intended to measure the performance of a clinical practice regarding that event.[4] This process is illustrated in Fig. 1. Variations in any of these steps will lead to different performance indicator scores. Ideally, data recorded for performance indicators are based on sound clinical practice guidelines, in which the definitions and inclusion and exclusion criteria of the performance indicator are clear and unambiguous and then processed in a uniform way to calculate the performance indicator in a uniform way. In reality, however, definitions are far from unambiguous and data are recorded in a variety of ways, impeding comparability of indicators for external quality control.[5, 6] This means that users of performance indicators need to be aware of the possible impact of variations in definitions and quality of the data in terms of availability, accessibility and completeness.[7, 8] The more unambiguous the definitions and the higher the quality of the underlying data, the more likely the performance indicator scores will be accurate and consistent between hospitals.[11]

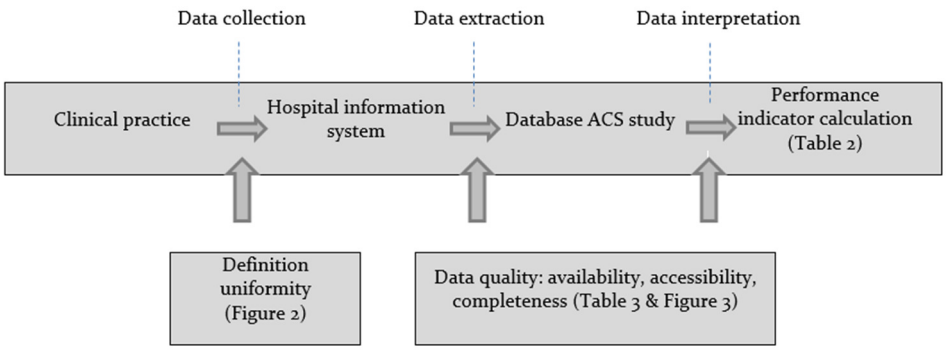

Figure 1. Comparability of data: flow from collection to interpretation.

For patients diagnosed with ST-segment elevation myocardial infarction (STEMI), international guidelines recommend timely invasive treatment by primary percutaneous coronary intervention (PCI), generally within 90 min of first medical contact.[1, 12] Delays in timely invasive treatment by PCI caused by, for example, residential distance rapidly decrease the benefits over alternative treatments,[13, 14] while shortening delays has the potential to contribute to decreased heart failure and mortality.[15, 16] It is, however, unclear to what extent the treatment delay indicator scores are comparable between hospitals. This study therefore aims to investigate to what extent variations in definitions influence performance indicator scores. Moreover, we investigate to what extent the quality of data in terms of availability, accessibility and completeness influences performance indicator scores. We conclude by providing recommendations for improving comparability of performance indicator scores.

METHODS

PATIENT DATA

Secondary data were used from two university hospitals and five tertiary teaching hospitals performing PCI participating in the acute coronary syndromes (ACS) program evaluation, within the larger national safety management program: 'VMS safety management program'.[2]

Data from these seven hospitals were collected manually by six chart abstractors using standardised case report forms. All abstractors had a background in research and received instructions for the chart review procedures by JT and JE. The chart abstractors collected data by means of retrospective review of the medical records in electronic or paper-based medical, nursing or catheterisation laboratory records of patients discharged between 1 January and 31 December 2012. Each month, eligible records of patients discharged in the preceding month were selected from the hospital billing system using the diagnosis treatment combination code. To determine the STEMI population, chart abstractors first considered all the records of patients diagnosed with ACS for inclusion. Next, the chart abstractors checked whether the discharge letter confirmed the ACS diagnosis. When the discharge diagnosis was unclear, the record was discussed with a cardiologist or other attending physician working in the field of cardiology. Charts of patients with a treatment delay not exceeding 6 h were included in the study.[9] Charts of patients without a discharge diagnosis of STEMI, those not undergoing an acute PCI, patients with secondary ACS (e.g. due to anaemia), those undergoing elective procedures, patients with missing or uninformative charts and

the charts of patients under the age of 18 years were excluded from the study. Chart abstractors signed a confidentiality agreement and all data were stored on a password protected network server of the VU University Medical Centre.

QUALITY INDICATOR DEFINITIONS

Five definitions for the treatment delay indicator were derived from literature (Table 1 and Fig. 2): (A) The Dutch 'VMS safety management program' guidelines[2]; (B) The adjusted Dutch 'VMS safety management program' evaluation[2]; (C) The mean door-to-needle time[9]; (D) The door-to-balloon time (American ACC/AHA guidelines for the management of STEMI[10, 12]); and (E) The European Society of Cardiology guidelines for the management of STEMI[1]. In these five definitions, treatment delay was defined as: (A) PCI within 90 min of first medical/paramedical contact; (B) PCI within 90 min of first electrocardiogram (ECG); (C) the mean door-to-needle time (no threshold provided); (D) PCI within 90 min of hospital arrival, and (E) PCI within 90 min after first medical contact. The B definition is an adaption of the A definition, because the time of first medical/paramedical contact was not registered consistently in all PCI centres but the time of the first ECG was. Thus, for this study, treatment delay was defined as the time from first ECG to PCI. Noteworthy is further that indicator C asks for the *mean* door-to-needle time, illustrating that different organisations ask hospitals to register different information. Moreover, although none of the PCI centres registered the time of wire passage in the culprit artery, which is used by the ESC in the last definition, we provide this definition as an illustration because these guidelines provide the basis for the first and second definitions. For this study, we regarded the time from first ECG to PCI as the reference standard for pragmatic reasons. We emphasise that this definition is not a gold standard as there is no common gold standard for measuring treatment delay due to national and international differences and differences in perceptions of stakeholders. Moreover, the definitions are used for comparison reasons and not to conclude what the best definition is.

Table 1 - Definitions for the performance indicator 'treatment delay'.	
A.	**VMSzorg.nl performance measure** *(source: VMS practice guide and VMS factsheet [2])*
Definition	Percentage of patients diagnosed with STEMI treated with PCI within 90 minutes of first medical/paramedical contact.
Numerator	All patients undergoing PCI treatment within 90 minutes of first medical/paramedical contact. Medical/paramedical contact is defined as the general practitioner, emergency medical services or emergency department. PCI treatment is defined as the time of sheath insertion.
Denominator	All patients diagnosed with STEMI
Inclusion	All patients diagnosed with STEMI
Exclusion	Patients with unstable angina or NSTEMI
B.	**Adjusted VMSzorg.nl performance measure** *(source: [2])*
Definition	Percentage of patients diagnosed with STEMI treated with primary PCI within 90 minutes of first ECG.
Numerator	All patients diagnosed with STEMI treated with primary PCI within 90 minutes of first ECG. If patients developed a STEMI while being hospitalised for another illness or symptom, the time of the first ECG with ST-segment elevation in hospital was registered. Start of PCI is defined as the time of sheath insertion.
Denominator	All patients diagnosed with STEMI treated with primary PCI
Inclusion	All patients with the diagnosis treatment combination code for ACS and discharge diagnosis of STEMI
Exclusion	STEMI patients undergoing pharmacological treatment or non-acute PCI (i.e. documented sub-acute or old infarction, ST-segment resolution on the electrocardiogram in combination with the absence of symptoms on admission); STEMI patients with >6 hours between ECG and PCI; patients with a secondary infarction (e.g. due to anaemia)
C.	**Dutch Health Care Inspectorate performance measure** *(source: [9])*
Definition	Mean door-to-needle time *Note: no threshold provided.*
D.	**ACC/AHA performance measure** *(source: [10])*
Definition 1	Median time from hospital arrival to PCI in AMI patients with ST-segment elevation or LBBB on the ECG performed closest to hospital arrival time
Definition 2	AMI patients with ST-segment elevation or LBBB on the ECG closest to arrival time receiving primary PCI during the hospital stay with a time from hospital arrival to PCI of 90 minutes or less
Numerator	AMI patients whose time from hospital arrival to primary PCI is 90 minutes or less.
Denominator	AMI patients with ST-segment elevation or LBBB on ECG who received primary PCI.

Table 1 continued - Definitions for the performance indicator 'treatment delay'.	
Inclusion	Discharges with: An ICD-9-CM Principal Diagnosis Code for AMI AND PCI (ICD-9-CM Principal or Other Procedure Codes for PCI) AND ST-segment elevation or LBBB on the ECG performed closest to hospital arrival AND PCI performed within 24 hours after hospital arrival
Exclusion	Patients less than 18 years of age Patients received in transfer from the inpatient, outpatient, or emergency department of another facility Patients given a fibrinolytic agent prior to PCI PCI described as non-primary by a physician/APN/PA Patients who did not receive PCI within 90 minutes and had a reason for delay documented by a physician, APN/PA (e.g., social, religious, initial concern or refusal, cardiopulmonary arrest, balloon pump insertion, respiratory failure requiring intubation)
E.	**ESC performance measure** *(source: [1])*
Description	…a target for quality assessment is that primary PCI (wire passage) should be performed within 90 min after FMC in all cases. In patients presenting early, with a large amount of myocardium at risk, the delay should be shorter (60 min). In patients presenting directly to a PCI-capable hospital, the goal should also be to achieve primary PCI within 60 min of FMC. Although no specific studies have been performed, a maximum delay of only 90 min after FMC seems a reasonable goal in these patients. Note that these target delays for implementation of primary PCI are quality indicators and that they differ from the maximal PCI-related delay of 120 min, which is useful in selecting primary PCI over immediate thrombolysis as the preferred mode of reperfusion

ACC/AHA American College of Cardiology and *American Heart Association*; *ACS* acute coronary syndromes; *AMI* acute myocardial infarction; *APN /PA* advanced practice nurses/ physician assistant; *ECG*: electrocardiogram; FCM flow cytometry; *ICM-9-CM* The *International* Classification of Diseases, Ninth Revision, Clinical Modification; *LBBB* left bundle branch block; *NSTEMI* non- ST-segment elevation myocardial infarction; *PCI* percutaneous coronary intervention; *STEMI* ST-segment elevation myocardial infarction; *VMS* safety management system

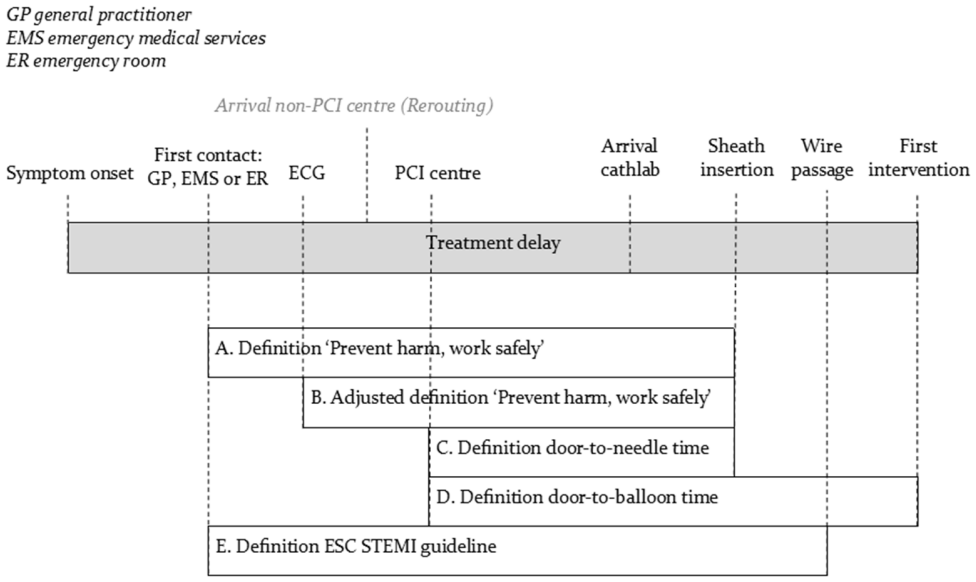

Figure 2 Delays from symptom onset to first intervention in patients with STEMI and five performance indicator definitions (A-E). *GP* general practitioner, *EMS* emergency medical services, *ER* emergency room.

OUTCOME MEASURES

DATA QUALITY

To investigate data quality (availability, accessibility and completeness), we assessed whether or not particular time points involved in the various definitions were recorded in each of the hospitals. If the data were recorded, the researcher noted how they were accessible. Accessibility was divided into three categories: (1) automatically accessible, (2) partly automatically accessible or (3) manually accessible.[5] Automatically accessible meant that data elements stored within the hospital information system could be easily reviewed ('only a few mouse clicks away') and extracted by means of computerised search algorithms. Partly automatically accessible meant that data elements were available in the hospital information system and could be reviewed easily, but could not be extracted by means of a computerised search algorithm and that manual actions were required. Manually accessible meant that data elements were available but only through intense data handling such as paper-based medical record reviews. Additionally, two chart abstractors retrospectively noted per hospital where and in what form data were found, such as in medical records, nurse records, discharge letters, electrocardiograms, procedure letters, correspondence with other health care professionals and in paper form, scanned or in the hospital information system. Finally,

we assessed the completeness of the available information at the patient level. We measured the percentage of patients for whom all time points that should be recorded were indeed available.

INFLUENCE OF DEFINITIONS ON INDICATOR SCORES

To investigate the influence of the performance indicator definition on the scores, we calculated the percentage of patients for whom the treatment delay indicator was below the threshold for each hospital according to the different definitions.

RESULTS

PATIENT DATA

Secondary data were used from two university hospitals and five tertiary teaching hospitals performing PCI. The bed capacity in these hospitals ranged between 400 to over 1100. Initially, 4471 records were reviewed for inclusion. After excluding records of patients who were not diagnosed with STEMI or excluded based on exclusion criteria ($n = 3454$), 1017 records were available for analyses, ranging between 112 and 236 included records per hospital.

OUTCOME MEASURES

DATA QUALITY

The chart abstractors reported that some hospitals recorded all the required data elements for the calculation of the performance indicator scores. Moreover, automated access to these data was not possible in most cases. The most common ways to access the data were manual or partly automated access (four of the seven hospitals). Fully automated access was not available for any of the data elements, illustrating that data collection was time consuming and costly.

For all available and accessible data, we noted where this information was found (Table 2). For the extraction of data elements with partly automated or manual access, the chart abstractors had to review a combination of medical records, nurse records, discharge letters, electrocardiograms (ECG), procedure letters, correspondence with other health care professionals, and in paper form, scanned or in hospital information system. Table 2 illustrates that the accessibility of data did not only differ per hospital, but also per time point within hospitals.

Table 2 - Data accessibility per hospital

	1	2	3	4	5	6	7
First contact	Care pathway registration / patient record (paper)	HIS	HIS	Scanned in HIS / cardiology department database	Care pathway registration / patient record (paper) / report in HIS	HIS	Patient record (paper)
ECG	Patient record (paper)	Scanned in HIS / cathlab system	Scanned in HIS	Scanned in HIS / cardiology department database	Patient record (paper) / scanned in HIS / care pathway registration	Scanned in separate folder on hard disk	Patient record (paper) / cathlab system
Arrival PCI centre	Patient record (paper)	HIS	HIS	HIS/ cardiology department database	Admission system	Separate database	Patient record (paper) / HIS
Sheath insertion	Cathlab report	Separate cathlab system	HIS	Cathlab report in HIS, or cardiology department database	Cathlab report / care pathway registration	Cathlab report in HIS	Cathlab system
First intervention	Cathlab report	Not available	HIS	Cardiology department database	Care pathway registration	Cathlab system	Cathlab system

HIS hospital information system

The completeness of the available information is illustrated in Fig. 3. In 24% of patients the time of first contact was recorded, in 88% of the patients the time of ECG, in 51% of patients the time of arrival at the PCI centre, in 94% of patients the time of sheath insertion and in 64% of patients the time of first intervention was recorded. Thus, hospitals vary greatly in completeness of recording, particularly with respect to the time of first contact.

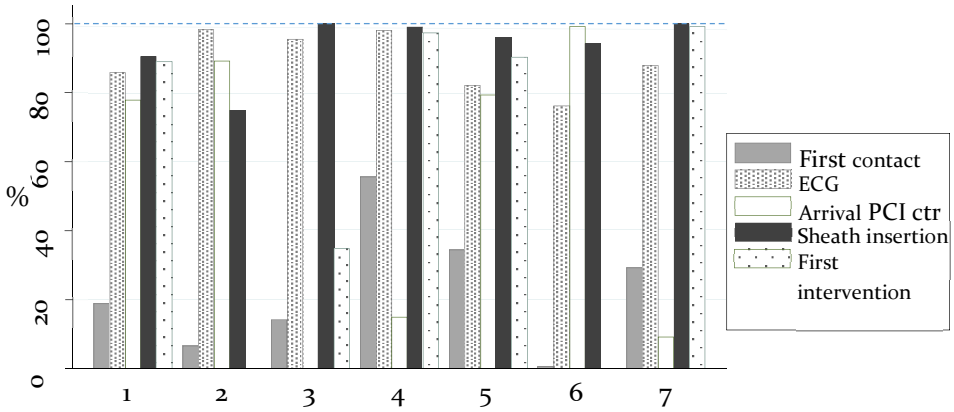

Figure 3. Completeness of time points per hospital.

INFLUENCE OF DEFINITION ON INDICATOR SCORES

Table 3 shows the percentage of patients satisfying the indicator threshold for each of the definitions and each of the hospitals. Indicator score B was reported best, with 15–50% missing data across hospitals. Missing data on indicator scores A, C and D were generally over 50% ranging from 21 to 100%. When calculable, indicator scores ranged from 57 to 100% within a given hospital, dependent on the indicator definition.

Table 3 - Time to PCI indicator: % of patents with missing data and number of times 90 min indicator was reached (*n yes; n total*) per definition per hospital.

Hospital (number) Definition of treatment delay	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**Total (patient with missing data % and indicator reached n)**
A. Dutch 'VMS safety management program' guideline	82% *13; 23*	93% n/a	86% 10; 16	44% 36; 63	69% 40; 56	99% n/a	71% 49; 69	85% 156; 236
B. Adjusted Dutch 'VMS safety management program' guideline	36% 81; 104	15% 102; 117	23% 86; 107	38% 69; 109	30% 119; 136	50% 70; 98	30% 165; 207	32% 692; 878
C.* Mean door-to-needle time (IGZ)	*91%* *11 (n=98)*	*85%* *18 (n=106)*	*100%* *n/a (-)*	*87%* *9 (n=15)*	*86%* *24 (n=137)*	*83%* *23 (n=131)*	*93%* *17 (n=22)*	*50%* *19 (n=509)*
D. Door-to-balloon time (ACC/ AHA)	24% 97; 98	100% n/a	100% n/a	86% 16; 16	21% 135; 136	100% n/a	91% 21; 22	74% 269; 272
Total (n of patients)	127	120	112	112	171	139	236	1017

n/a data for indicator not available or fewer than 10 cases
* Indicator asks for mean door-to-needle time
IGZ Dutch Health Care Inspectorate

DISCUSSION

This study illustrates that hospital performance indicator scores for the treatment delay performance indicator are largely incomparable, without laborious manual review. Three reasons contribute to this incomparability. First, definitions vary for treatment delay performance indicators across the literature, which leads hospitals to vary in the extent to which different time points are recorded and/or used for calculating performance indicators. These differences are also due to the low number of patients and missing data. This is partly due to the choices hospitals make regarding which times to record, but also due to the format in which organisations compel hospitals to report indicators (as percentage or mean). To compare indicator definitions among patients with all data points would be a methodologically sound method. In practice, information is not available for all the data points in any of the patients, as hospitals use different definitions for treatment delay and vary greatly in the extent to which the necessary data are available, accessible and complete. So, this leads to substantially different indicator scores, especially between definitions A and B versus D. Second, the chart abstractors reported that some hospitals had all the required data elements for calculation of the performance indicators and data could not be retrieved easily in any of the hospitals. Moreover, data accessibility not only varied between hospitals, but also between data elements within hospitals. The same hospital could therefore have a relatively low indicator score following one definition and relatively a high score following another definition. Third, we found large variations between hospitals in completeness of time records.

Previous studies on the comparability of medical data in the Netherlands and across Europe similarly showed that required data elements for performance indicators were generally poorly available, accessible and incomplete.[5, 10, 17, 18] This may partly be due to the enormous number of indicators hospitals have to report on for external quality control. In order to compare indicator scores among hospitals it is thus necessary to standardise definitions and record data uniformly, and possibly reduce the number of indicators that hospitals have to accurately measure.[19, 20]

To obtain structured data, predefined computer-based forms to record relevant procedures and findings in a structured, standardised format, have been shown to be advantageous.[21] One way to convert the currently used open text into a more structured format is the use of Natural Language Processing tools. However, as most tools are developed in English, further research is required on how to handle the Dutch.

Moreover, to enhance the correctness of data items and thus efficiency of secondary use of data, the Netherlands Federation of University Medical Centres is detailing how to best apply the 'collect once—use many times' principle.[22] A next step could be to automatically extract data quality items from the hospital information system, checked by a responsible party and submitted to quality registers or other authorised parties.[20] Ideally, data that are in standard codes from comprehensive controlled clinical terminologies such as SNOMED CT can be reused automatically. In the Netherlands, an action plan was recently developed to create a standardised continuity of care record for Dutch hospitals and to create semantically sound subsets of terminologies using SNOMED CT and ICD 10.[20] Moreover, the USA initiated a nationwide taskforce Meaningful Use of Complex Medical Data in order to overcome problems analysing large amounts of medical data in a timely fashion.[23] Today, hospital performance data can be linked to national mortality databases to provide information on long-term outcomes and survival, provided data can be tracked across providers, which is facilitated by unique person identifiers.[24] Such a national registry is not available for acute coronary syndromes in the Netherlands, whereas this has been possible for many years in other countries, such as Sweden and the UK.[25] Given these advances, performance indicators based on administrative data could be a very useful tool to flag possibilities for quality improvement in hospitals. The extent of these propositions, however, does not provide practitioners with a direct, simple solution. The proposed statements include steps which need to be taken in order to prevent incomparability in the future. Hospital associations in the Netherlands are now working on these steps. Despite the lack of solutions, we feel it is important to inform practice of the critical notion that hospital performance indicator scores for the treatment delay performance indicator are largely incomparable, without laborious manual review.

Our study has several limitations. The time points extracted to calculate indicator scores per hospital may be an overestimation of data completeness compared with indicator scores calculated and supplied by hospitals themselves, because data were extracted by chart abstractors who went to great lengths to obtain data. Moreover, the data obtained by our chart abstractors may deviate from hospital data as the chart abstractors made decisions to clarify which data were necessary to calculate performance indicator scores, such as manually checking all diagnoses in the discharge letter based on the diagnosis and procedure codes. Also, the presence of researchers collecting data on site and the provision of feedback of performance may have influenced documentation of times and performance indicator scores. However, as the patient safety program for which

the data were primarily collected was designed to improve guideline adherence and provide hospitals with feedback of their own performances, it would not be appropriate to withhold this information. Consequently, another limitation is the secondary use of data that were obtained for the goal of measuring guideline adherence. For example, the exclusion of uninformative charts means that data were preselected on their quality. In spite of these limitations, our results show that the comparability of indicator scores is influenced by data quality issues.

CONCLUSION

In sum, hospitals use different definitions of this one particular quality indicator and vary greatly in the extent to which the necessary data are actually available, accessible and complete, impeding comparability between hospitals. It is important to increase awareness among developers, users and producers of performance indicators regarding the impact of variations in indicator definitions and data quality on indicator scores.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

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Chapter 5

Multi-centre analysis of current ST-elevation myocardial infarction acute care pathways

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ABSTRACT

Background: Rapid reperfusion with percutaneous coronary intervention (PCI) is vital for patients with ST-segment elevation myocardial infarction (STEMI). However, the guideline-recommended time targets are regularly exceeded. The goal of this study was to gain insight in how Dutch PCI centres try to achieve these time targets by comparing their care processes with one another and with the European guideline-recommended process. In addition, accelerating factors perceived by care providers were identified.

Methods: In this multiple case study, interviews with STEMI care providers were conducted, transcribed and used to create process descriptions per centre. Analyses consisted of within-case and between-case analyses of the processes. Accelerating factors were identified by means of open and axial coding.

Results: In total, 28 interviews were conducted in 6 PCI centres. The centres differed from the guideline-recommended process on e.g. additional, unavoidable patient routings and monitoring delays, and from one another on the communication of diagnostic information (e.g. transmitting all, only ambiguous or no electrocardiograms) and catheterization room preparation. These differences indicated diverging choices to maintain a balance between speed and diagnostic accuracy. Factors perceived by care providers as accelerating the process included trust in the tentative diagnosis, and avoiding unnecessary inter-caregiver consultations. The combination of processes and accelerating factors were summarized in a model.

Conclusions: Numerous differences in processes between PCI centres were identified. Several time saving strategies were applied by PCI centres, however in different configurations. To further improve the care for STEMI patients, best practices can be shared between centres and countries.

INTRODUCTION

Rapid reperfusion treatment increases the chances of survival for patients with ST-segment elevation myocardial infarction (STEMI).[1, 2] Consequently, international STEMI care guidelines recommend to limit the time to treatment with percutaneous coronary intervention (PCI) to a maximum of 90 minutes from first (para)medical contact.[3, 4] However, previous studies reported that attaining these time targets is difficult.[5]

In the European Society of Cardiology guidelines, a model of care has been described to treat patients within 90 minutes after first (para)medical contact. In this description, patients contact the emergency medical services through a central telephone number. In case of a suspected myocardial infarction, the emergency medical services dispatch an ambulance. In the ambulance, an electrocardiogram is recorded and interpreted by trained paramedics, and/or the electrocardiogram is transferred for a teleconsultation with a cardiology centre. Triage, diagnosis and emergency treatment are all performed in the prehospital phase. The cardiology centres, with 24/7 PCI services, cooperate with other hospitals in the region and with the emergency medical services through clear geographic boundaries, shared protocols and bypassing of non-PCI hospitals. While the patient is en route to the hospital, the catheterization laboratory staff are called and the room is prepared. On arrival, the patient bypasses the emergency department and intensive coronary care unit and is immediately transferred to the catheterization laboratory. The treatment delays are measured and used to improve the process of care.

Despite the before mentioned guideline-recommended process, the recommended maximal treatment delay of 90 minutes is still exceeded for a considerable number of patients in the Netherlands.[6] Although treating all patients within the recommended time targets is unlikely, there appears room for improvement. In addition to a well-designed process, hospital, patient and physician related factors including annual PCI volume and time of presentation appear to influence the speed of the care process as well.[7] Therefore, further optimizing the logistic processes and taking into account accelerating factors may reduce the treatment delay and subsequently lower the patients' risk of adverse cardiac events.[8] Therefore, the primary objective of this study was to explore how PCI centres in the Netherlands differed in their logistic processes from the European guideline-recommended process and from one another. The secondary objective was to identify factors potentially accelerating the process.

METHODS

DESIGN

As quantitative information about the delays in the acute STEMI care process is lacking in many countries including the Netherlands, [9, 10] the study was performed in a multiple case study design, using PCI centres as cases. This type of design is well suited for exploring and comparing complex processes in a real life context.[11]

SETTING

The study was conducted in the Netherlands, a country of approximately 34,000 km^2 where annually more than 11.000 patients are treated with primary PCI in 30 PCI centres.[12] Due to an efficient geographical spread of PCI centres in the Netherlands, PCI is the preferred reperfusion therapy for all patients with STEMI who present within 12 hours of symptom onset. Therefore, timely provision of fibrinolysis was not taken into account in this study.

To access a PCI centre, patients may take different routes. In the Dutch healthcare system, the general practitioner has a gatekeeping role, meaning that referral from a general practitioner is required to see a hospital physician. Exceptions are made for medical emergencies such as STEMI, but some patients with symptoms of STEMI contact their general practitioner or general practitioners' after-hours office. In their guidelines for acute coronary syndrome, general practitioners are recommended to call the emergency medical services and perform an anamnesis and physical examination.[13]

Alternatively, patients can contact the emergency medical services in the Netherlands directly by dialling the national emergency number (112). If indicated by the triage system, an operator of 1 out of 25 self-dispatching regional ambulance services sends an ambulance to the patient. Ambulances are staffed by a driver and by a nurse licensed to administer medical treatment at advanced life support level.[14] All ambulance services work according to a national ambulance protocol which allows for regional adaptations in cooperation with the PCI centres.[15] This protocol describes to transport patients with a (tentative) STEMI diagnosis directly to the nearest PCI centre.[16] As a result of these national structures, the treatment delay in this study was defined as the period from first (para)medical contact in person to the PCI procedure. In addition, the care process was defined as all statements pertaining to individual tasks and responsibilities that contributed to getting the patient to a prepared catheterization room.

SELECTION OF PCI CENTRES AND PARTICIPANTS

In total, 7 hospitals providing primary PCI 24/7 were invited to participate in the present study after participating in a previous study, for which they were selected using a multi-stage random selection procedure.[17] These PCI centres differed among other things in ambulance region, annual PCI volume and type of hospital (University vs non-University teaching). At each centre, an interventional cardiologist specialized in acute coronary syndromes was invited by e-mail for an interview. In the interviews, cardiologists were asked to provide contact details of one person from each profession involved in acute STEMI care at the hospital or at the emergency medical services. These professionals were subsequently approached by email to participate in the study. Additionally, for verification of the information given about the additional prehospital care processes, cardiologists from referring hospitals and general practitioners were invited for participation through the interventional cardiologist.

DATA COLLECTION

Data were collected by means of one-on-one semi-structured interviews at the workplace or home of the participant. The interviews were conducted with a topic list based on the European guideline-recommended process.[3] The topic list was tested in two pilot interviews and adjusted accordingly, resulting in a final topic list (Supplemental Table 1). Each interview started with a grand tour question in which cardiologists were asked to describe the care process from symptom onset to reperfusion for patients with STEMI going for primary PCI. Subsequent questions were related to the steps in the care process described by the participant, the role of other care providers in the process, prior quality improvement efforts, and monitoring of the guideline-recommended time targets.

The interviews were performed by one interviewer, trained in qualitative interviewing (JT), between May 2013 and February 2014, were audio-recorded and transcribed verbatim using the computer program F4 2012 (Version 5.2, Dr Dresing & Pehl GmbH - audiotranskription.de).

DATA ANALYSES

In analysing the process of STEMI care, the data reduction strategy of Miles & Huberman for multiple case studies was used.[18] Within-case and between-case analyses were performed with the care process for STEMI patients in the PCI centres as the unit of analysis. First, all interview transcripts were reviewed line-by-line and split into three

predetermined process steps: 1) first (para)medical contact in person to PCI decision; 2a) activation of the catheterization room; and 2b) PCI decision to start of the PCI procedure. Process steps 2a and 2b occur simultaneously. Use of additional strategies to reduce the treatment delay are mentioned separately. Next, the care process per PCI centre, taking into account different patient routings, was described in detail (within-case analysis). The textual and graphical descriptions (swim lane charts) were linked by using similar annotation. An example of a swim lane chart describing the general process of prehospital care is presented in Supplemental Figure 1. Differences of the logistic processes of PCI centres with the European guideline-recommended process and with one another were identified by comparing the textual and graphic process descriptions (between-case analysis).

Factors accelerating the care process but not pertaining to it were identified by reviewing all transcripts line-by-line. All issues related to accelerating factors as indicated by the participants were extracted from the transcripts and coded by means of open coding (content analysis). Subsequently, text fragments with similar open codes were bundled in an axial coding process and their contents were analysed inductively to reveal the core categories of factors accelerating the care processes.

After conducting and transcribing 12 interviews (covering all PCI centres), JT performed an interim analysis in which additional care providers in the process and potential gaps in the descriptions of the process per PCI centre were identified. To improve the reliability of the coding scheme, 3 interviews were coded independently by a second researcher [IvdW] and differences in the coding were discussed until consensus was reached. As a result, small modifications to the definitions in the coding scheme were made accordingly.

All transcripts were coded using the computer program ATLAS.ti (Version 5.2, ATLAS.ti Scientific Software Development GmbH).

VERIFICATION

The textual and graphical process descriptions of each PCI centre were sent back to the participating interventional cardiologists for verification. All interventional cardiologists responded, resulting in minor changes in the process descriptions.

ETHICAL APPROVAL

This study was approved by the medical ethical committee of the VU University medical centre. All participants were informed about the study goals and data processing, and written consent for study participation and audio recording of the interview was obtained. Data were stored on a password protected network drive of the VU University medical centre, to which only the researchers had access. Codes were assigned to participants and centres for privacy purposes. Additionally, all transcripts were anonymised by removing all names of people, centres and geographical locations.

RESULTS

From 6 PCI centres, 25 care providers were interviewed (Table 1). One centre did not respond to the invitation and could therefore not be included. Moreover, to verify the general prehospital care process, 2 general practitioners and 3 cardiologists from referring hospitals were invited for participation, of whom 1 general practitioner and 2 cardiologists participated. This resulted in a total of 28 interviews with a mean duration of 45 minutes (range: 23 to 68 minutes).

Table 1. Characteristics of participating PCI centres and interview participants

Hospital	**a**	**b**	**c**	**d**	**e**	**f**
Type of hospital	Teaching	Teaching	Academic	Teaching	Teaching	Teaching
Provision of thoracic surgery	No	Yes	Yes	No	Yes	Yes
Number of catheterization rooms (primarily for PCI)	2 (1)	5 (3 or 4)	3 (2)	2 (1)	5 (2 or 3)	3 (2)
Number of primary PCI procedures per year	300-400	>500	400-500	<300	>500	>500
Interventional cardiologist	x	x	x	x	x	x
Cardiology resident		x	x		x	x
Catheterization room nurse	x	x	x	x	x	x
Cardiac care unit nurse	x		x	x		
Ambulance nurse/medical manager	x	x	x	x	x	x
*Referring cardiologist**				x		x
*GP**			x			

*participants in *Italic* for verification; PCI: percutaneous coronary intervention

DIFFERENCES FROM THE EUROPEAN GUIDELINE-RECOMMENDED PROCESS AND BETWEEN PCI CENTRES

Differences between the care processes of individual PCI centres, the European guideline-recommended process, and between PCI centres could be allocated to one of the process steps below. Differences between PCI centres are summarized in the lower part of Figure 1. Illustrative quotes are presented in Supplemental Table 2 and referred to in the text. The letters between brackets in the text correspond to the letters for the PCI centres presented in Table 1.

FIRST (PARA)MEDICAL CONTACT IN PERSON TO PCI DECISION

The prehospital care processes of the PCI centres differed from the European guideline-recommended process on one aspect. The European guideline-recommended process assume that patients arrive at the catheterization room from the emergency medical services. In this study, additional patient routings were identified in which patients were already admitted to a hospital department, e.g. the surgery department; or presented to emergency departments of PCI centres or non-PCI centres. The cooperation with the ambulance services was highly protocolled, while the cooperation with the general practitioners, emergency departments, other hospital departments or referring hospitals was much less protocolled. In case patients go to the general practitioner, no electrocardiogram is performed and the emergency medical services are contacted immediately.

Between PCI centres, several differences were found. When patients are announced at the PCI centre by the emergency medical services, the emergency department or referring hospitals, there can be uncertainty or ambiguity about the working diagnosis. However, additional diagnostic tests might result in a prolonged treatment delay. The PCI centres differed in the way they dealt with the trade-off between diagnostic certainty and speed. Some PCI centres had dedicated facilities to receive prehospital electrocardiograms transmitted from the ambulance, followed by a telephone call (**a**,**b**,**c**,**f**). This provided the possibility for a coronary care unit nurse (**a**) or cardiology resident (**b,c,f**) to confirm the diagnosis. After hours, in one centre (**c**) all electrocardiograms were additionally forwarded to the interventional cardiologist on call for review. Other centres had no dedicated facilities for electrocardiogram reception, but occasionally electrocardiograms were received through (protected) mobile phone applications (**d**,**e**). One PCI centre was able to receive electrocardiograms, however, not all ambulance service providers in the region were equipped to transmit electrocardiograms (**b**), leading to variation within the region.

In case there were facilities for transmitting and receiving electrocardiograms (**a**,**b**,**c**,**f**), different criteria were used for the decision to employ these facilities. Some PCI centres required all electrocardiograms to be transmitted (**a**,**c**), while others only required ambiguous electrocardiograms to be transmitted (**b**,**f**), thereby minimizing the number of consultations for unambiguous diagnoses (Quote 1). In the PCI centres where only the ambiguous electrocardiograms were transmitted or which had no dedicated facilities to receive electrocardiograms, the patient was always accepted for angiography and PCI without additional diagnostic testing or consultation when an ambulance nurse indicated with certainty the patient had a STEMI (**b**,**d**,**e**,**f**) (Quote 2). As a result, no electrocardiograms were transmitted and the PCI centre was only contacted by telephone to convey additional information about the patient. In one centre (**a**), the decision to send a patient for PCI was made by a dedicated coronary care unit nurse, while in another centre (**c**) a cardiology resident made the decision. In case the diagnosis was uncertain, a cardiology resident or interventional cardiologist could be consulted, resulting in additional discussion before the patient was accepted.

ACTIVATION OF THE CATHETERIZATION ROOM

In all PCI centres included in this study, the catheterization room was activated by a dedicated care coordinator at the PCI centre. The profession of the care coordinator differed between PCI centres. In one centre (**a**), the coordinator was a dedicated nurse from the coronary care unit both during office hours and after hours. The nurse had the autonomy to read the electrocardiogram and activate the catheterization room without additional consult of a cardiologist or cardiology resident (Quote 3). In three centres, during office hours a cardiologist activated the catheterization room while after hours a cardiology resident (**b**,**f**) or coronary care unit nurse (**d**) was responsible. In two other centres, the cardiology resident was always responsible for catheterization room activation (**c**,**e**). However, in one of these centres (**c**) a coronary care unit nurse was contacted first through a landline, who subsequently transferred the call to the cardiology resident, resulting in an additional process step. The difference in profession of the care coordinator indicates different choices between speed (a readily available nurse) and reliability of the diagnosis (a more difficult to reach cardiologist).

During office hours, the catheterization room staff was already present as they performed elective PCI procedures and thus the catheterization room systems were already operational. When an incoming patient required primary PCI, ongoing or planned elective procedures in one of the catheterization rooms were cancelled and

rescheduled to free the room for the incoming patient. Up to the point where a sheath or guidewires were inserted, patients undergoing elective procedures were removed from the catheterization room to speed up its availability.

After hours, the catheterization room staff on call (interventional cardiologist and multiple catheterization room nurses) were generally not present at the centres. There were two exceptions. One centre required all staff on call that had to travel over 20 minutes to the centre to stay overnight (**f**), while at another centre some cardiologists stayed overnight voluntarily (**e**). The catheterization room staff staying overnight at the centre initiated catheterization room preparations immediately after announcement of the patient, thereby optimally using the transport time of the patient. At two centres (**a**,**b**), preparation of the catheterization room was initiated by a coronary care nurse working evening- or nightshift while the catheterization room staff and patient were en route to the centre (Quote 4).

An addition to the European guideline-recommended process was found in the way the catheterization room staff was contacted after hours. The interventional cardiologist and catheterization room nurses were called by the care coordinator or doorman to present to the PCI centre within 20 to 30 minutes. None of the centres used a single-call page system but contacted the staff by (mobile) telephone instead, enabling immediate confirmation. To start the procedure as soon as possible, only the interventional cardiologist and at least one catheterization nurse had to be present.

PCI DECISION TO START OF THE PCI PROCEDURE

As recommended in the European guideline, the emergency department was bypassed upon arrival at the hospital and the patients were transported directly to the catheterization room on the ambulance stretcher. When the catheterization room was not available yet patients were accommodated to a holding area near the catheterization room or to the coronary care unit. In contrast to the European guideline-recommended process, in one centre the patients made an additional stop at the coronary care unit (**d**) (Quote 5), from where a coronary care unit nurse transported the patient to the catheterization room. The nurse stayed to assist in the procedure and transported the patient back to the coronary care unit to facilitate continuity of care.

In case the catheterization room was not ready upon arrival of the patient at the PCI centre, several strategies for accommodating the patient were identified. Some PCI centres had a dedicated holding area for patients awaiting catheterization at the catheterization room complex on the ambulance stretcher (**a**,**b**), while others admitted patients at the coronary care unit (**c**,**f**,**e**). One centre sporadically set up these patients at another catheterization room, so that only the staff had to change rooms (**b**).

MONITORING OF DELAYS

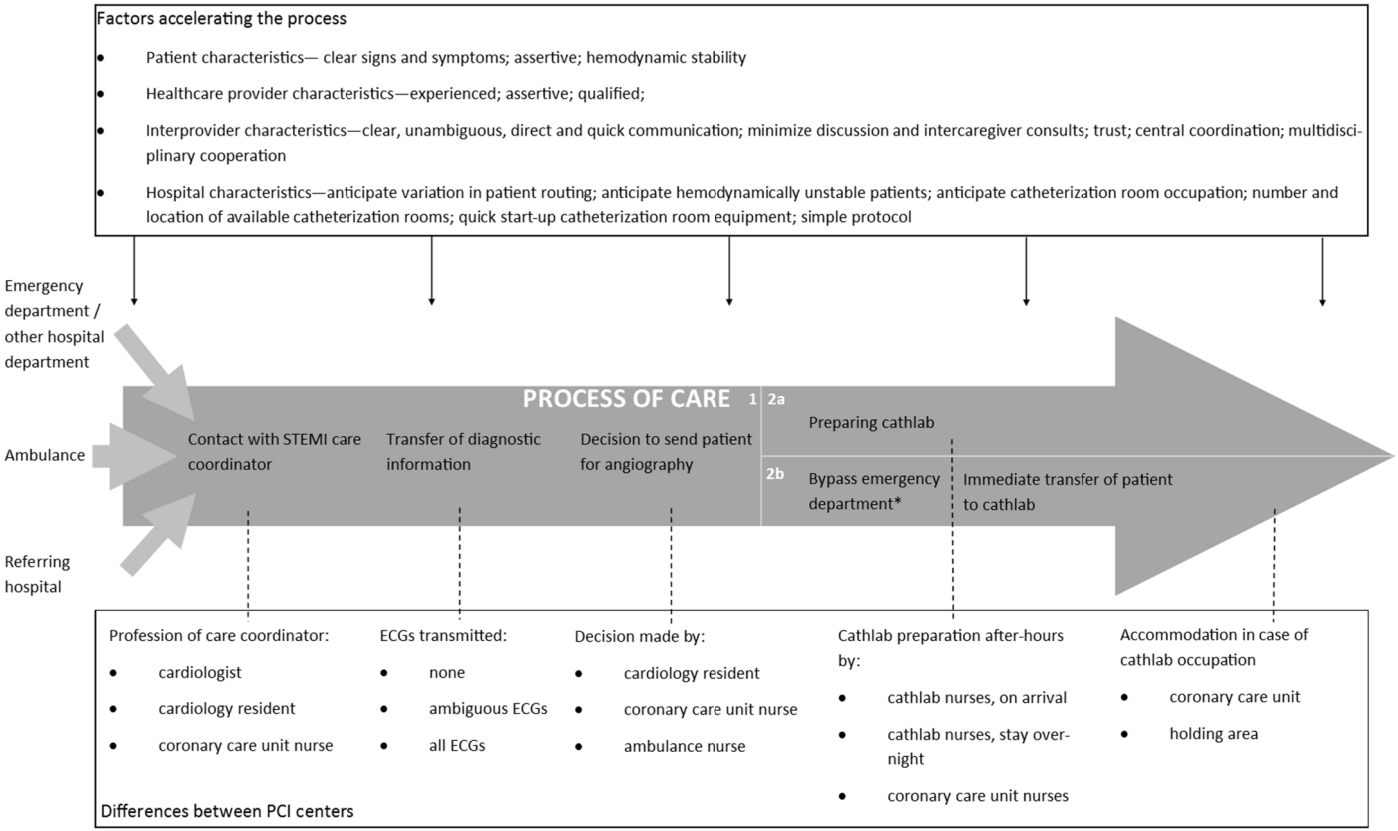
An additional strategy in the European guideline-recommended process was to monitor the treatment delays and identify variation. However, only one PCI centre used this strategy (**a**), though, all centres recorded information about the treatment delay to report on national quality indicators.

ACCELERATING FACTORS

Several factors not pertaining to the process were identified by the healthcare providers as accelerating the care process. These factors were categorized as patient, healthcare provider, inter-provider and PCI centre characteristics and are summarized in the upper part of Figure 1.

PATIENT CHARACTERISTICS

Participants mentioned that the *clarity of the signs and symptoms* experienced by the patient determines the way patients interpret their complaints, and the care provider that they contact. The participants indicated that bypassing the general practitioner and calling the emergency medical services directly accelerated the care process. Furthermore, in contacting a care provider, the *patient's assertiveness* can influence the priority that he/she is being given, e.g. by insisting that the complaints are severe. Additionally, when patients are *hemodynamic stable* fewer resources i.e. equipment, care providers (e.g. anaesthesiologist) and diagnostic procedures (e.g. an ultrasound) are required, which accelerates the process.



* Irrelevant in case the emergency department was the first medical contact for the patient); 1: from first (para)medical contact to PCI decision; 2a: activation of the cathlab; 2b: PCI decision to start of the PCI procedure

Figure 1. A model of variation and accelerating factors in the process of acute care chain of STEMI patients going for primary PCI

HEALTHCARE PROVIDER CHARACTERISTICS

A working diagnosis is the starting point for the PCI centre to initiate preparations for receiving a STEMI patient. Therefore, the working diagnosis needs to be made prehospital by an *experienced* and *qualified* diagnostician in order to make a reliable diagnosis to ensure activation of the catheterization room without further diagnostic testing (Quote 6). Also, participants indicated that in the communication with the PCI centre, it is vital that the diagnostician is *assertive* in case he/she is certain of the working diagnosis of STEMI in order to avoid additional transfer of information and unnecessary consultations. Consequently, in some centres a cardiology resident had to consult the interventional cardiologist, in which the same factors of experience, qualification and assertiveness are important for the cardiology resident, thereby limiting the potential delay caused by the additional consultations.

INTERPROVIDER CHARACTERISTICS

In case the working diagnosis is made, the communication between the ambulance crew and the PCI centre needs to be *clear*, *quick*, *unambiguous* and *direct*. Participants stressed that this will *minimize discussion* about the diagnosis, resulting in a shorter treatment delay. One important requirement is *trust* in the diagnosis made by the ambulance nurse or other diagnostician. When trust in the diagnosis is high, no further discussion is needed and preparations for the PCI procedure can be initiated (Quote 7).

However, doubt about the working diagnosis can result in additional *intercaregiver consults* in which the diagnosis is discussed, potentially delaying catheterization room activation and patient transport. Therefore, *multidisciplinary cooperation* in minimizing doubt about the diagnosis and agreeing on an acceptable level of uncertainty in the region of a PCI centre is deemed as an important factor accelerating the process in the long run.

PCI CENTRE CHARACTERISTICS

The *catheterization room location* should ideally be near the ambulance entrance, the emergency department and the coronary care unit of the PCI centre to limit transfer times. In addition, *having multiple catheterization rooms* increases the chances that one is available. Having *catheterization room equipment with a short start-up time* as well as a *having a simple protocol* describing everyone's responsibilities can reduce the time to prepare the catheterization room.

Anticipating on different patient routings and characteristics was identified by the participants as important for optimizing the process speed. For example, some PCI centres *anticipate on transporting hemodynamically unstable patients to the catheterization room as soon as the patient is stable enough*. The cardiologist goes to the emergency department immediately after prehospital notification to provide care and to remind other care providers that the patient needs to go to the catheterization room as soon as possible. At the catheterization room, specialized staff (e.g. anaesthesiologist) with advanced equipment are waiting to take care of the patient. PCI centres also *anticipated on catheterization room occupancy* by having a dedicated holding area near the catheterization room.

DISCUSSION

In this study, the care processes in multiple PCI centres for patients with STEMI going for primary PCI in the Netherlands were compared to the European guideline-recommended process and to one another. In addition, factors accelerating the process were determined. The PCI centres differed from the European guideline-recommended process on additional, unavoidable patient routings and monitoring delays. Differences between PCI centres included the way diagnostic information was communicated and having personnel ready on-site to immediately prepare the catheterization room. Accelerating factors included the patients' assertiveness, trust in the diagnosis of colleagues and avoiding inter-caregiver consultations and discussion.

In all PCI centres, the emergency medical services bypassed the emergency department upon arrival at the hospital. This is in accordance to previous study results, in which direct transport to the catheterization room was identified as a time-saving strategy.[19] However, the procedures for patients entering the PCI centres through alternative routings were less protocolized. Therefore, it is important that in optimizing the care process, PCI centres take into account all patient routings in shared protocols and infrastructure for all involved care providers in their region. Continuously updating and disseminating the guideline-recommended process enables individual PCI centres to compare their own process with the synthesis of best practices. Additional improvements in comparison to our model can be shared within and between STEMI care networks. [20]

In the design of the acute care process for patients with STEMI, PCI centres appeared to seek a balance between accuracy of the diagnosis and speed of the process. While

some centres chose for a system in which the ambulance nurse decided to send the patient for PCI, other centres chose for a system in which the electrocardiogram first had to be evaluated by a coronary care unit nurse, cardiology resident or interventional cardiologist. This additional verification of the diagnosis may result in a prolonged treatment delay, while on the other hand it may prevent unnecessary catheterization room activations. Previous studies indicated proficient interpretation of electrocardiograms by emergency medical services staff,[21, 22] indicating that transmittal of the electrocardiogram might not be required.[23] However, transmitting the electrocardiogram allows for comparison to previous electrocardiograms, thereby potentially minimizing unnecessary catheterization room activation.[24] An optimal configuration of the care process may be identified by means of computer simulation, in which the effect of an altered configuration on the treatment delay and the diagnostic certainty can be evaluated. Computer simulations have been applied in decreasing patient wait times at the emergency department, [25] and could also be of value in optimizing the treatment delay.
Although driving times are prolonged in Denmark, a higher number of procedures per operator was linked with improved patient outcomes.[26]

The optimal level of centralization of primary PCI procedures within countries remains unclear. Although driving times can be shorter in a more decentralized approach, a more centralized approach can result in a higher number of PCI procedures per operator. Both aspects of care have been linked to improved patient outcomes, [2, 26] but they appear mutually exclusive. To gain insight in an optimal centralization strategy, a natural experiment can be used, e.g. by comparing patient outcomes in the Netherlands and Denmark. Denmark, with 5.6 million inhabitants on 43.000 km^2 and approximately 2700 primary PCI procedures each year [12], is comparable to the Netherlands on both the terrain, infrastructure and guideline recommendations. [27-30] The major difference appears the number of PCI centres providing primary PCI procedures: 30 PCI centres for 16.8 million inhabitants (560.000 inhabitants per PCI centre) in the Netherlands versus 4 PCI centres for 5.6 million inhabitants (1.4 million inhabitants per PCI centre) in Denmark. In addition, the organization of the emergency medical services (25 regions in the Netherlands versus 5 regions in Denmark) is also more centralized. It is unclear to what extent this further centralization of STEMI care influences patient outcomes. It would therefore be recommendable to compare patient outcomes between the Dutch and Danish systems in order to identify an optimal level of centralization.

The accelerating factors could be organized in four categories: patient, provider, inter-provider and PCI centre characteristics. In reducing the treatment delay, it appears crucial to redesign the process while taking into account factors that may influence the speed of the process. Although not all factors can be influenced directly by care providers, anticipating situations in which these factors play a role may help to minimize treatment delays e.g. having an adapted process for hemodynamically unstable patients. In addition, both provider and inter-provider characteristics are mentioned as accelerating the process. These categories justify multidisciplinary training within a region in order to align the views of all involved care providers, including general practitioners, referring hospitals and emergency department staff. Taking into account these accelerating factors may further decrease the treatment delay in the long run.

The differences in the care processes and the accelerating factors are presented as independent factors, while in real life they may be interrelated. For example, when an interventional cardiologist trusts the diagnosis made by an ambulance nurse or coronary care unit nurse, no further discussion is required. This trust can in turn be influenced by the experience and qualification of the diagnostician and by the clarity of the patients' signs and symptoms. Low trust in the diagnosis might result in additional discussion or an additional stop at the emergency department for further diagnostic testing, prolonging the treatment delay. Consequently, in optimizing the process it is important to consider both process steps and accelerating factors.

STUDY LIMITATIONS

The study results should be interpreted taking potential limitations into consideration. Personal views and experiences of participants may have affected the reliability of data collected by means of interviews. The accelerating factors were perceived by the care providers and not tested quantitatively and should therefore be interpreted with caution. To increase the reliability of the data, a variety of PCI centres and care providers per PCI centre and its region were included.

The data were collected in a single country, which may have influenced the usability of the study findings for other countries. However, the care of patients with STEMI has been standardized in international cardiology guidelines and primary PCI is the reperfusion method of choice in many countries.[10] Therefore the findings of this study can be useful internationally, though differences in the national protocols or accelerating factors may occur.

In the present study, no professionals from the emergency department were interviewed. This was because cardiologists and cardiology residents were closely involved in the care for patients with a suspected cardiac disease at the emergency department. In addition, in the Netherlands only a very small number of patients arrive through the emergency department. Strategies to optimize care for STEMI patients that focus on the emergency department will therefore have limited effect in reducing the average treatment delay in a hospital. However, a part of the process was not directly explored in the present study which could have affected the reliability of the reported results.
Finally, we were unable to link the processes identified per PCI centre in this study to time intervals or patient outcomes because of size differences between the regions in which centres were located which may affect the treatment delay. As a consequence, it cannot be determined to what degree the reported process differences and accelerating factors accounted for a shorter treatment delay. However, the overall treatment delay in the participating centres was relatively short [6] compared to other studies, and multiple time-saving strategies as identified in previous best practices were applied in all PCI centres, e.g. prehospital diagnosis and bypassing the emergency department [9].

CONCLUSIONS

Several differences of the current acute care process for STEMI patients in comparison to the European guideline-recommended process and between PCI centres were found. These differences potentially affect the treatment delay, indicating room for further improvement. Hospitals can learn from each other's process designs by identifying and sharing best practices. The results of this study therefore facilitate future quality improvement efforts and research that may eventually reduce the treatment delay of patients with STEMI.

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COMPETING INTERESTS

None

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CONTRIBUTORS

JT designed the study; collected, analysed and interpreted the data; and wrote the initial draft of the paper. CdB and IvdW helped analyse and interpret the data and revised subsequent versions of the paper. MdB and CW helped design the study and revised subsequent versions of the paper.

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Chapter 6

Adherence to guidelines for the prescription of secondary prevention medication at hospital discharge after acute coronary syndrome: a multicentre study

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ABSTRACT

Background: The prescription of guideline-recommended medication for secondary prevention after acute coronary syndrome has been suboptimal in the past. In the present study, guideline adherence and associated patient, care and hospital characteristics at hospital discharge after acute coronary syndrome were studied.

Methods: Charts of patients with acute coronary syndrome discharged from 13 Dutch hospitals in 2012 were reviewed. Guideline adherence was defined as the prescription of acetylsalicylic acid, P2Y12 receptor inhibitor, statin, beta-blocker and angiotensin-converting enzyme (ACE) inhibitor at discharge, or a documented contraindication. Associated characteristics were identified by means of generalized linear mixed models for binary outcomes.

Results: In total, 2471 patients were included. Complete guideline adherence was achieved in 69.1% of the patients, ranging from 42.1 to 87.0% between hospitals. The ACE inhibitor was most often missing (21.2%). Patients with non-ST-segment elevation myocardial infarction or unstable angina, patients with a history of coronary artery bypass grafting or elderly women were less likely to be discharged with the guideline-recommended medication.

Conclusions: Guideline adherence for secondary prevention medication following acute coronary syndrome was substantial; however, variation between hospitals and patient groups was found. Efforts to increase guideline adherence can focus on underperforming hospitals and undertreated patient groups.

BACKGROUND

In recent years, the in-hospital survival rates of patients with an acute coronary syndrome (ACS) have increased[1], yet patients with a history of ACS are at higher risk of adverse cardiac outcomes in the future[2]. As a result, discharge and post-discharge management, comprising referral to a cardiac rehabilitation program and the prescription of secondary prevention medication[3, 4], have become more important in ACS care.

Prescribing medication for secondary prevention of adverse cardiac outcomes after discharge from the hospital is recommended by the European Society of Cardiology guidelines on the management of ACS. This medication comprises a combination of acetylsalicylic acid, P2Y12 receptor inhibitor, statin, beta-blocker and angiotensin-converting enzyme (ACE) inhibitor[3, 4] However, previous studies have identified non-adherence to these guideline recommendations in several patient groups.[5, 6] As a result, these patients have a higher but potentially preventable risk of adverse outcomes after discharge.[7]

Monitoring and improving guideline adherence for secondary prevention medication at hospital discharge has the potential to improve the quality of care and further reduce adverse outcomes in patients with ACS.[8, 9] This was recognised by Dutch cardiology care providers, who included a focus on discharge medication in a national quality improvement program.[10] In this study we investigated guideline adherence and associated patient, care and hospital characteristics for secondary prevention medication at discharge from the hospital for patients with ACS in the Netherlands during implementation of a nationwide quality improvement program.

METHODS

A detailed description of the study design, methods and the quality improvement program has previously been published.[11]

DESIGN

The study was conducted in a cross-sectional design.

SETTING AND INCLUSION

In 2012, 91 hospitals provided ACS care in the Netherlands. From this pool, 13 hospitals were selected by means of a multistage random sampling procedure to participate in the evaluation of the national quality improvement program.

Potentially eligible study charts were selected from the hospitals' financial system codes for ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina (UA). All patients discharged in 2012 with a diagnosis of ACS (as confirmed in the discharge letter) were considered for inclusion. Charts of patients transferred to another hospital or department for further evaluation or treatment, patients who died during hospital admission, who received palliative care, who left the hospital against medical advice or who had no information about the prescribed medication at discharge in their chart were excluded.

DATA COLLECTION AND PROCESSING

Data were collected by means of retrospective chart review. The chart reviewers visited the participating hospitals monthly. When the number of charts exceeded the screening capacity, charts were selected per month in chronological order of discharge until the screening capacity limit was reached.

In this study, guideline adherence was defined as the prescription of acetylsalicylic acid, P2Y12 receptor inhibitor, statin, beta-blocker and ACE inhibitor at discharge, or a documented contraindication or other motivation for not prescribing these medicines. From the charts, information related to the prescription of these five medicines was abstracted. In case one or more medicines were not prescribed, documented contraindications as reported in an annually updated Dutch database of pharmacotherapy[12], or as motivated by the treating physician were retrieved (e.g. the prescription of anticoagulants instead of acetylsalicylic acid). The full list of contraindications was reported previously.[11] Additionally, patient, care and hospital characteristics ($n = 40$), e.g. age, sex, cardiac medical history, risk factors, resuscitation and discharge diagnosis were recorded. Hospitals were characterised by type (academic, tertiary teaching or general) and presence of percutaneous coronary intervention (PCI) and/or coronary artery bypass grafting (CABG) facilities (yes/no).

A sample of the charts ($n = 149$ (6.0%)) was screened by two chart reviewers independently and the percentage of agreement between the reviewers was calculated. The results were satisfactory, with all 40 variables above 85% agreement indicating good to excellent data reliability.

MISSING DATA

In total, 0.82% of the data were missing, ranging per variable from 0.04% (date of discharge) to 2.5% (heart failure or arrival). Little's test[13] was non-significant ($p = 0.57$) and missing value analyses showed no relationship between the missing data and the complete data, indicating the missing data were missing completely at random.[14] Therefore missing data were imputed by means of full conditional specification using the imputation procedure in IBM SPSS (Version 20 for Windows). As a sensitivity analysis, the results of the final analysis were compared with the results of a full case analysis to determine the accuracy of the imputation procedure.

ANALYSIS

Characteristics of the study population, participating hospitals and guideline adherence were determined by means of descriptive statistics. Associations of predictor variables with guideline adherence (complete adherence vs incomplete adherence) were studied by means of generalized linear mixed models for binary outcomes. To correct for clustering of patients within hospitals, hospital was entered as random effect in the analyses.

The associations of the predictor variables with guideline adherence were tested in univariate models (Table 1). All predictor variables with a significant association ($p \leq 0.05$) were added to a multivariable model. To account for collinearity, all predictor variables without a significant association in the univariate analyses were added to the multivariable model one by one. In case of a significant improvement of the model fit ($p \leq 0.05$), they were added to the multivariable model. Additionally, several potential interactions between variables were tested in the multivariable model: age with treatment, discharge diagnosis and sex; and discharge diagnosis with treatment and sex. In case of a significant improvement of the model fit ($p \leq 0.05$), the interactions were added to the multivariable model. From this model, the fixed effects were presented as odds ratios (OR) with 95% confidence intervals (CI).

Associations of patient, arrival, discharge and hospital characteristics with prescription of discharge medication in univariable generalized linear mixed models ($N = 2471$).

The data were analysed in R (version 3.0.2 for Windows) using the *lme4* package.

Table 1. Associations of patient, arrival, discharge and hospital characteristics with prescription of discharge medication in univariable generalized linear mixed models (N=2471)

Variable	n (%)	Incomplete guideline adherence (n=763)	Guideline adherence (n=1708)	P-value[1]
Discharge diagnosis				***<0.001
STEMI	910 (36.8%)	161 (21.1%)	749 (43.9%)	
NSTEMI	987 (39.9%)	310 (40.6%)	677 (39.6%)	
UA	574 (23.2%)	292 (38.3%)	282 (16.5%)	
Type of treatment				***<0.001
Medication	793 (32.1%)	355 (46.5%)	438 (25.6%)	
PCI	1552 (62.8%)	360 (47.2%)	1192 (69.8%)	
CABG	126 (5.1%)	48 (6.3%)	78 (4.6%)	
Age in years (mean, 95% CI)	66.9 (66.4-67.4)	65.9 (65.3-66.5)	69.1 (68.1-70.0)	***<0.001
Female	801 (32.4%)	287 (37.6%)	514 (30.1%)	***<0.001
Admission				
Resuscitation	100 (4.0%)	9 (1.2%)	91 (5.3%)	***<0.001
Heart failure on arrival	138 (5.6%)	35 (4.6%)	103 (6.0%)	0.29
Cardiogenic shock on arrival	35 (1.4%)	11 (1.4%)	24 (1.4%)	0.79
Transportation from another hospital	394 (15.9%)	97 (12.7%)	297 (17.4%)	**0.002
Discharge				
Month of discharge	N/A	N/A	N/A	0.22
Weekend discharge	724 (29.3%)	226 (29.6%)	498 (29.2%)	0.85
Length of stay (median days, 1st-3rd quartile)[2]	5 (3-7)	5 (4-7)	4 (3-6)	***<0.001
Risk factors				
Diabetes mellitus	545 (22.1%)	118 (15.5%)	427 (25.0%)	***<0.001
Hypertension	1204 (48.7%)	389 (51.0%)	815 (47.7%)	0.10
Kidney failure	111 (4.5%)	22 (2.9%)	89 (5.2%)	*0.02
Chronic heart failure	103 (4.2%)	31 (4.1%)	72 (4.2%)	0.61
Positive family history	910 (36.8%)	281 (36.8%)	629 (36.8%)	0.64
Coronary stenosis	205 (8.3%)	79 (10.4%)	126 (7.4%)	**0.003
Hyperlipidaemia[3]	1208 (48.9%)	375 (49.1%)	833 (48.8%)	0.61

Table 1 continued. Associations of patient, arrival, discharge and hospital characteristics with prescription of discharge medication in univariable generalized linear mixed models (N=2471)

Variable	n (%)	Incomplete guideline adherence (n=763)	Guideline adherence (n=1708)	P-value[1]
Obesity (BMI>30 kg/m^2)	270 (10.9%)	80 (10.5%)	190 (11.1%)	0.64
Smoker	739 (29.9%)	184 (24.1%)	555 (32.5%)	***<0.001
Former smoker	452 (18.3%)	138 (18.1%)	314 (18.4%)	0.99
Cardiac medical history				
Angina pectoris	442 (17.9%)	167 (21.9%)	275 (16.1%)	**0.001
Peripheral vascular disease	159 (6.4%)	50 (6.6%)	109 (6.4%)	0.69
Coronary artery disease	264 (10.7%)	96 (12.6%)	168 (9.8%)	*0.03
Prior MI	574 (23.2%)	189 (24.8%)	385 (22.5%)	0.21
Prior PCI	592 (24.0%)	206 (27.0%)	386 (22.6%)	*0.02
Prior CABG	303 (12.3%)	125 (16.4%)	178 (10.4%)	***<0.001
Recent PCI, CABG or MI (<6 months before admission)	142 (5.7%)	42 (5.5%)	100 (5.9%)	0.51
Hospital characteristics				
Type of hospital				0.26
General hospital (n=4)	648 (26.2%)	245 (32.1%)	403 (23.6%)	
Tertiary teaching hospital (n=7)	1426 (57.7%)	430 (56.4%)	996 (58.3%)	
Academic hospital (n=2)	397 (16.1%)	88 (11.5%)	309 (18.1%)	
Treated in hospital with PCI facilities (n=7)	1512 (61.2%)	448 (58.7%)	1064 (62.3%)	0.73
Treated in hospital with CABG facilities (n=5)	958 (38.8%)	290 (38.0%)	668 (39.1%)	0.87

STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; UA, unstable angina pectoris; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CI, confidence interval; N/A, not applicable; BMI, body mass index; MI, myocardial infarction

[1] P-values are calculated using the Wald statistic, comparing the model fit of a generalized linear mixed model with and without the variable, corrected for clustering of patients in hospitals

[2] Length of stay was log transformed after careful consideration of the residuals of a model without random intercept

[3] Hyperlipidaemia was defined as described in patients history or statin use before admission

* significant at ≤0.05 level; ** significant at ≤0.01 level; *** significant at ≤0.001 level

ETHICAL APPROVAL

The study protocol was approved by the medical ethics review committee of the VU University medical centre.

RESULTS

SELECTION OF PATIENT CHARTS

In total, 3427 charts of patients with a confirmed discharge diagnosis of ACS in 2012 were screened. Of these, 876 patients (26.6%) were transferred to another hospital or department for further evaluation or treatment, 56 (1.6%) died during admission, information concerning discharge medication was missing for 14 patients (0.4%), 6 (0.2%) left the hospital against medical advice and 4 (0.1%) received palliative care. After exclusion of these charts, 2471 patients were eligible for further analyses. Their mean age was 66.9 years and the majority were male (67.6%) (Table 1).

GUIDELINE ADHERENCE

Overall, 49.1% of the patients were prescribed all five guideline-recommended medicines at discharge from the hospital, while an additional 20.0% had contraindications documented for the medicines that were not prescribed. Consequently, the complete guideline adherence for the combination of the five medicines was 69.1%. Guideline adherence for the individual medicines ranged between 99.6% for acetylsalicylic acid and 76.8% for the ACE inhibitor. Complete guideline adherence for the combination of the five medicines ranged from 42.1 to 87.0% between hospitals. Prescription rates and guideline adherence are presented in Table 2 and Fig. 1.

Table 2. Prescription patterns for the five medicines for secondary prevention (N=2471)

Drug type	Prescriptions n(%)	Range (% in lowest – highest scoring hospital)	Guideline adherence [1] n(%)	Range (% in lowest – highest scoring hospital)
Acetylsalicylic acid	2271 (91.9%)	86.6%-97.2%	2460 (99.6%)	98.6%-100%
P2Y12 receptor inhibitor	2189 (88.6%)	70.3%-95.9%	2293 (92.8%)	75.7%-98.6%
Statin	2294 (92.8%)	81.1%-97.4%	2363 (95.6%)	83.8%-98.9%
Beta-blocker	2220 (89.8%)	83.5%-99.0%	2360 (95.5%)	90.5%-99.0%
ACE inhibitor	1603 (64.9%)	47.5%-74.5%	1898 (76.8%)	57.9%-93.1%
All 5 medicines	1214 (49.1%)	28.2%-59.0%	1708 (69.1%)	42.1%-87.0%
4 out of 5 medicines	2068 (83.7%)	67.8%-91.0%	2297 (93.0%)	78.4%-99.0%

ACE, angiotensin-converting enzyme; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; UA, unstable angina pectoris
[1] Guideline adherence refers to either prescription of the medicine or documentation of a contraindication

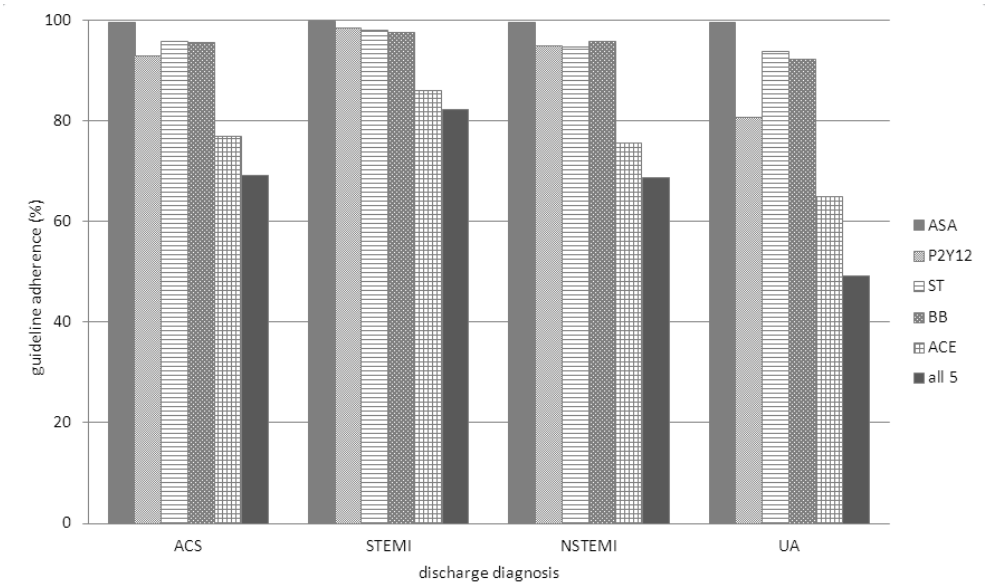

Fig 1. Guideline adherence (%) per medicine per discharge diagnosis. ASA=acetylsalicylic acid; P2Y12=P2Y12 receptor inhibitor; ST=statin; BB=beta-blocker; ACE=angiotensin-converting enzyme inhibitor; ACS=acute coronary syndrome; STEMI=ST-elevation myocardial infarction; NSTEMI=non-ST-elevation myocardial infarction; UA=unstable angina

FACTORS ASSOCIATED WITH (IN)COMPLETE GUIDELINE ADHERENCE

In univariate generalized linear mixed model analyses, discharge diagnosis, type of treatment, age, sex, resuscitation, transport from another hospital and length of stay were significantly associated with the probability of guideline adherence (Table 1). Additionally, the risk factors diabetes mellitus, kidney failure, a prior detected coronary stenosis, current smoking, and a medical history of angina pectoris, coronary artery disease, prior PCI or prior CABG were associated with the probability of guideline adherence. These were entered in a multivariable model. The variable 'recent PCI, CABG or myocardial infarction (<6 months before admission)' significantly improved the multivariable model fit and was therefore subsequently added to the model secondarily. In addition, an interaction between age and sex was added to the multivariable model. No significant associations between hospital characteristics and guideline adherence were found.

In the final model, patients with NSTEMI or UA compared with patients with STEMI, and patients who had a prior CABG were less likely to receive the guideline-recommended medication at discharge (Table 3). Further, adherence was higher for patients who were treated with PCI compared with patients who received pharmacological or CABG treatment, who had diabetes mellitus or kidney failure, who were resuscitated on admission, who had longer lengths of hospital stay, or who had a recent PCI, CABG or myocardial infarction (<6 months before admission). Additionally, the effect of age differed between men and women, i.e. the medication was less likely completely according to the guidelines for older women compared with older men.

Table 3. Associations of patient, arrival, discharge and hospital characteristics with prescription of secondary prevention medication in the multivariable generalized linear mixed model

Variable	OR (95% CI)	P-value
Discharge diagnosis		
STEMI (intercept)	N/A	0.37
NSTEMI	0.64 (0.49 - 0.82)	***<0.001
UA	0.29 (0.21 - 0.39)	***<0.001
Female patient	4.09 (1.32 - 12.7)	**<0.01
Coronary artery disease	1.13 (0.79 - 1.61)	0.51
Angina pectoris	1.04 (0.79 - 1.38)	0.76
Prior PCI	0.98 (0.76 - 1.26)	0.87
Prior CABG	0.70 (0.51 - 0.95)	*0.02
Diabetes mellitus	2.67 (2.06 - 3.45)	***<0.001
Kidney failure	2.10 (1.23 - 3.57)	*0.007
Smoker	1.19 (0.94 - 1.50)	0.16
Coronary stenosis	0.82 (0.56 - 1.20)	0.30
Resuscitation	2.65 (1.29 - 5.44)	**0.008
Transportation from another hospital	0.81 (0.60 - 1.10)	0.18
Age	0.97 (0.96 - 0.99)	***<0.001
Length of stay [1]	1.43 (1.19 - 1.72)	***<0.001
PCI	2.05 (1.63 - 2.59)	***<0.001
CABG	0.98 (0.63 - 1.55)	0.94
Recent PCI, CABG or MI (<6 months before admission)	1.91 (1.23 - 2.95)	**0.004
Interaction between Age and Sex	1.02 (1.00 - 1.04)	**0.003

STEMI, ST-segment elevation myocardial infarction; N/A, not applicable; NSTEMI, non-ST-segment elevation myocardial infarction; UA, unstable angina pectoris; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; MI, myocardial infarction

[1] Length of stay was log-transformed after careful consideration of the residuals of a model without random intercept

* significant at ≤0.05 level; ** significant at ≤0.01 level; *** significant at ≤0.001 level

SENSITIVITY ANALYSIS

As a sensitivity analysis the current model was compared with a full case analysis model ($n = 2253$). No differences were found in variable selection or significant associations, indicating a reliable imputation procedure.

DISCUSSION

In this multicentre study, guideline adherence for secondary prevention medication prescription at hospital discharge for patients with ACS was investigated. Complete guideline adherence was 69.1%, with the highest adherence for acetylsalicylic acid and the lowest for the ACE inhibitor. Several patient and care characteristics were significantly associated with guideline adherence, while hospital characteristics were not.

The level of complete guideline adherence found in this study was comparable with another Dutch study in which 65.2% of the patients with ACS were discharged with the recommended secondary prevention discharge medication.[15] Also, in accordance with other studies, guideline adherence for the recommended discharge medication was lowest for the ACE inhibitor.[16] This finding may be explained by the recommendation to prescribe the ACE inhibitor to all patients with ACS, but an exception may be made for normotensive patients without heart failure, left ventricular (LV) dysfunction or diabetes mellitus.[4] Furthermore, an angiotensin-II-receptor inhibitor can be prescribed as an alternative for the ACE inhibitor, although the ACE inhibitor is the primary choice, as previous studies showed superiority in reducing adverse outcomes.[17] Therefore, prescription of an angiotensin-II-receptor inhibitor was not abstracted from the charts in this study.

Although there was substantial variation in guideline adherence between hospitals, this could not be explained by the hospitals' characteristics (presence of intervention facilities and type of hospital). A recent study found that hospitals with interventional facilities treated more patients according to the guidelines.[15] The different findings in this study might be explained by the use of a statistical correction for clustering of patients in hospitals, thereby reducing the effective sample size.[18] When no statistical correction for clustering is used, the hospital characteristics are attributed to individual patients ($n = 2471$) instead of hospitals ($n = 13$), resulting in spurious significant results.

The odds of complete guideline adherence were lowest for patients with UA, intermediate for NSTEMI patients and highest for patients with STEMI. This finding confirms the results of previous studies.[19, 20] The difference in guideline adherence between STEMI and NSTEMI/UA might be explained by small differences in the European Society of Cardiology guidelines for the management of ACS patients with and without ST-segment elevation. One difference is the recommendation to prescribe a beta-blocker to all patients with STEMI, while only to patients with NSTEMI/UA who have LV dysfunction. However, this difference in the guidelines does not explain the differences found in the present study, as the differences between STEMI and NSTEMI/UA were mostly caused by lower guideline adherence for the ACE inhibitor and the P2Y12 receptor inhibitor. Moreover, the high prescription rates of beta-blockers in NSTEMI and UA patients might indicate overmedication or adherence, potentially caused by adherence to previous guidelines[21] as guideline adoption takes time.

Interestingly, the negative association of age with guideline adherence was stronger in women than in men. This finding is worrisome, as the most recent European guidelines recommend managing both genders in a similar fashion.[22] To our knowledge, there is limited information on the impact of sex and age on the decision of physicians to prescribe secondary prevention medication after acute coronary syndrome. Therefore, additional research is required to identify potential (reasons for) treatment biases of physicians towards treatment of elderly women.

Since the estimated guideline adherence for secondary prevention medication after ACS was substantial, it would be recommended to focus future quality improvement efforts on reducing variation between patient groups and between hospitals. Several interventions exist for improving guideline adherence, e.g. feedback of performance[23], continuing education[24] or integrated care[25]. These interventions can focus on undertreated patient groups, e.g. facilitating educational meetings for cardiology care providers about the treatment of elderly women with ACS.

LIMITATIONS

Several limitations of this study might influence interpretation of its results.

Having no information on one of the medicines prescribed at discharge in the patient chart can be the result of no prescription, or no documentation of the prescription, contraindication or another reason for not prescribing the medicine (e.g. preserved

LV function for the ACE inhibitor). As the charts were not screened by physicians, implicit decisions could not be included in the chart review. Instead, a standard list of contraindications was used, thus minimising inter-reviewer variation. Consequently, the rates of guideline adherence in this study might differ slightly from real-life guideline adherence and are therefore only an estimate. An additional limitation relating to documentation is the selection of patients by means of the hospital billing systems with manual review of the discharge diagnosis in the chart. Potentially some ACS patients were missed who received a billing code not related to ACS or with a different discharge diagnosis documented in their chart, which could limit the external validity of the findings in this study.

Another limitation of this study was that the potential prescription of suboptimal doses of medicines was counted as adhering to the guidelines.[26] As optimal doses tend to differ between patients, and the optimal dose can often not be prescribed at discharge, it was not possible to incorporate doses in this study. Counting suboptimal doses as guideline adherence may have led to an overestimation of the quality of care in this study. In addition, prescribing medicines that are not indicated can also be considered to be incomplete guideline adherence. However, as the charts were not screened by physicians, this could not be taken into account in this study.

Prescription behaviour of individual physicians can be an additional source of variation in guideline adherence[27]; however, in this study it was not feasible to identify the physician responsible for medication prescription at discharge from the charts.
As a result of the large number of patients in PCI centres, the screening capacity limited the number of included patient charts per month. However, this should not have affected the results in our study since patients were selected in chronological order of discharge and there was no difference in guideline adherence between hospitals with and without PCI and/or CABG facilities.

Finally, participation in a national quality improvement program and the monthly measurements might have overestimated guideline adherence. However, the effect of this program on guideline adherence is expected to be limited as no significant association between month of discharge and guideline adherence was found.

CONCLUSION

Guideline adherence concerning the prescription of discharge medication in the Netherlands is substantial though differs between hospitals and patient groups. Efforts to further improve guideline adherence can be targeted on those patient groups who receive suboptimal treatment at discharge from the hospital, e.g. elderly women and patients with NSTEMI or UA.

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CONFLICT OF INTEREST

None declared.

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Chapter 7

Interventions to improve guideline adherence of care providers in hospitals in the management of patients with acute coronary syndrome and their effects: a systematic review

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Submitted for publication

ABSTRACT

Background: Improving guideline adherence in the process of care for patients with acute coronary syndromes has a strong link with improved patient outcomes. However, improving guideline adherence is difficult, as many interventions can be used, either stand-alone or combined into more complex interventions. The aim of this review is to identify intervention components used to improve the guideline adherence in the process of ACS care; to identify their effectiveness; and to identify whether combining multiple components is more effective than single or two components.

Methods: In this review, the Cochrane Effective Practice and Organisation of Care methodology was followed where appropriate. A systematic search was performed in PubMed, EMBASE, CINAHL, PsycINFO, the Cochrane Library and ABI/INFORM. All studies aiming to improve guideline adherence in the process of ACS care were included. After providing an overview of study characteristics, the studies with the strongest research designs ((cluster) randomized trials, controlled before-after studies and interrupted time series) were included. The studies were summarized and effects of interventions were estimated.

Results: The systematic search resulted in 4560 unique papers. In total, 265 studies aimed to improve guideline adherence in the process of ACS care. Most studies attempted to improve pharmaceutical prescription or timely invasive or thrombolytic intervention. After selecting the strongest study designs, 24 studies were included and summarized and assessed for risk of bias. In these studies, the most common intervention components were audit and feedback, educational interventions, educational materials and local opinion leaders. Combining three or more components appeared more effective in improving the ACS care process.

Conclusions: In most studies, similar components were used. Combining multiple component interventions appeared more effective in improving the care process of patients with ACS. The most effective intervention appeared a combination of audit and feedback, educational materials and meetings, and continuous quality improvement.

INTRODUCTION

Adhering to (inter)national guideline recommendations in the hospital management of patients with acute coronary syndromes (ACS) is important as it prevents cardiac damage and improves chances of survival.[1, 2] Lower guideline adherence can result in a higher risk of dying, especially in elderly patients.[3] Because of the positive association between guideline adherence and patient outcomes, measuring guideline adherence is an important tool for identifying room for improvement in the quality of care in clinical practice.

Several studies showed that guideline adherence has been suboptimal in ACS care, indicating large differences between individual patients [4], hospitals [2] and countries [5]. For example, the prescription of medication at discharge and treating patients within the recommended treatment delays were suboptimal.[6, 7] Although there should always be room to deviate from guideline recommendations in order to adapt a treatment to individual patient characteristics and needs, interventions with the goal to increase guideline adherence have led to improved patient outcomes in the past.[8] This finding indicates that deviating from the guidelines is not always beneficial. Therefore, quality improvement programs aiming to stimulate guideline adherence are implemented on local, regional, national and international levels.

Improving guideline adherence is difficult however, and various interventions have been applied in the past. In the field of research on guideline implementation, multiple types of interventions or intervention components have been proposed, e.g. education in continuous quality improvement and feedback of the performance in treatment delay.[9, 10] However, it is unclear what interventions are used in practice and what interventions were effective in improving guideline adherence in the management of patients with ACS. In addition, combining multiple intervention components into more complex interventions might be more effective than using one or two intervention components. The aims of this study were therefore to 1) provide an overview of studies aiming to improve guideline adherence in ACS hospital care; 2) identify the intervention components in the studies with the strongest research design and evaluate their effectiveness; and 3) assess whether combining multiple intervention components is more effective than single or double component interventions. This study will provide policy makers with a comprehensive overview of interventions aiming to improve guideline adherence in ACS care, and hence facilitate effective quality improvement efforts.

METHODS

DESIGN

In this systematic review of the literature, interventions applied to improve guideline adherence in the treatment of patients with ACS were identified. The Cochrane Effective Practice and Organisation of Care (EPOC) methods for systematic reviews were used where appropriate.

SEARCH STRATEGY

The search strategy was set up by JT in cooperation with a library information specialist of the VU University medical centre, and contained terms for acute coronary syndromes, guideline adherence and hospital care (Additional file 1, not included in this thesis). The following electronic medical research databases were searched: PubMed, EMBASE through Embase.com, CINAHL through EBSCO, PsycINFO through EBSCO and the Cochrane Library through Wiley (up to April 2014). For studies from the field of operations management the electronic business research database ABI/INFORM was searched through ProQuest. Additionally, experts in the fields of cardiology, guideline adherence and quality improvement for patients with ACS (n=17) were approached by email to identify relevant studies. References of potentially relevant articles and narrative reviews, and potential result publications of published study designs were screened for additional citations.

INCLUSION AND EXCLUSION CRITERIA

Studies were included when one or more of their research questions or research objectives were to improve the process of ACS care by increasing guideline adherence (e.g. improving performance on process quality indicators) among health care professionals in hospitals. All guidelines by professional cardiology organizations worldwide (e.g. American College of Cardiology/American Heart Association, European Society of Cardiology or the Japanese Circulation Society) and process quality indicators were considered. Consequently, the primary or secondary outcome variable(s) of the included studies were measures of guideline adherence or process quality indicator scores.

Articles were excluded when the study did not evaluate the effectiveness of an intervention to increase guideline adherence, or no results of quantitative data analyses were presented (e.g. editorials, research protocols or qualitative studies). When multiple articles were published about the same study, only the main article about the effect of the intervention on guideline adherence was included. From systematic reviews, the

relevant primary studies were included. No articles were excluded based on their year of publication.
The titles and abstracts of all citations found in the electronic databases or referred to by the experts were screened by two raters independently (JT and IvdW). The citations were categorized as inclusion, exclusion or unclear. In case the citation was marked as unclear by either rater, it was discussed until consensus on in- or exclusion was reached. When no consensus was reached, a third rater (MdB) was consulted.

OVERVIEW OF STUDIES

After the first screening on title and abstract, the papers were reviewed in-depth by retrieving the full-text where possible and screened for inclusion or exclusion. To provide an overview of the preliminary included studies, basic elements of these studies were extracted: study design, the processes which the intervention aimed to improve, the number of hospitals that participated and the number of ACS patients included. For the citations where no full-text could be obtained (n=22), the information was extracted from the abstract. Data extraction was initially performed by two reviewers independently (JT and SvS) until the definitions in the data extraction tool were adequate and the agreement between the two reviewers was satisfactory; afterwards the data extraction was performed by a single reviewer (JT).

DATA EXTRACTION

From the studies included in the overview, only studies with the study designs recommended by EPOC were included in the final study selection: (cluster) randomized controlled trials; controlled before-after studies with at least more than 1 intervention site; and interrupted time series with at least three measurements before and after the intervention (as recommended by the EPOC group). From these studies, the design, methods (including a description of the intervention and its components according to the EPOC framework[11], Table 1) and results were recorded. The risk of bias of individual studies was estimated using the EPOC suggested risk of bias criteria[12], as appropriate for (cluster) randomized trails/controlled before-after studies or interrupted time series. All information was recorded in evidence tables (Additional file 2, not included in this thesis). The description of the intervention components and study outcomes are additionally described in the results section of this paper.

Table 1. Summary of the main categories of the Effective Practice and Organisation of Care (EPOC) framework

Delivery arrangements	**Financial**
How and when care is delivered	Collection of funds
Where care is delivered	Insurance schemes
Who provides care	Mechanism of payment
Coordination and management	Targeted financial incentives
Information and communication technology	**Governance arrangements**
Implementation	Authority and accountability for policies
Interventions targeted at organizations	Authority and accountability for organizations
Interventions targeted at professionals	Authority and accountability for commercial products
Interventions targeted at specific types of practices	Authority and accountability for professionals

In this table, only the main categories are described. Each main category has multiple subcategories, for example implementation interventions aimed at professionals includes audit & feedback, local consensus processes, etc.

DATA SYNTHESIS

During our systematic review, it was found that either the number of patients was not reported per process measure, or only the number of hospitals was reported. Consequently, no confidence intervals or pooled effect sizes could be calculated. Therefore, synthesis was performed by averaging the overall effectiveness of the interventions in the studies. The overall effectiveness was calculated by averaging the difference in performance (%) between the intervention and control groups post-intervention for all included process measures reported as percentages in the study. Overlapping outcome measures (e.g. overall performance scores) were excluded to avoid double counting. To assess the effectiveness of relatively simple versus more complex interventions, studies with ≤2 component interventions were compared with ≥3 component interventions. To reduce potential effects of sampling variation, smaller studies (an arbitrary 1000 patients included in the study) were excluded from average effectiveness calculations.

RESULTS

Searches in the electronic databases yielded 5815 citations. These results were supplemented with 576 citations recommended by the experts in the fields of quality improvement research in cardiology. After deduplication, 4560 unique citations were screened, of which 582 citations were about improving guideline adherence in ACS care. After excluding studies in which no quantitative data were reported, 265 papers met our

inclusion criteria and basic study characteristics from these papers were extracted. Most of these studies aimed to improve pharmaceutical prescription, time to percutaneous coronary intervention or time to thrombolysis. Few studies aimed to improve use of risk scoring instruments, risk assessment or referral to cardiac rehabilitation (Table 2).

Table 2 Care process measure and number of studies

Study subject	# of times studied*
Pharmaceutical prescription	133
Time to percutaneous coronary intervention	104
Time until thrombolysis	78
Other	51
Referral to smoking cessation	43
Time until diagnosis	36
Use of diagnostic instruments / use of interventional therapy	31
Referral to cardiac rehabilitation	23
Risk assessment	17
Use of risk scoring instruments	5

* multiple process measures per study could be reported.

The majority of the studies were performed with a non-controlled before-after design (Table 3). In ten papers, the study design not mentioned or described in a way that did not allow for identification of the study design and were therefore excluded. Figure 1 shows the flow chart of the study selection.

Table 3 The study design of the included studies for in-depth review

Study design	# of times used
Non-controlled before-after study	181
Case series	32
Cohort study	14
Cluster randomized controlled trial	11
Controlled before-after study	12
Randomized controlled trial	4
Interrupted time series	1
Unclear	10

From the studies included in the overview, 241 studies were excluded on research design or because there were multiple publications about the same study. In total, 24 studies met our criteria, from which in-depth information was abstracted and the risk

of bias was assessed. The studies were performed in different designs: 4 randomized controlled trials; 11 cluster randomized controlled trials; 8 controlled before-after studies and 1 interrupted time series study.

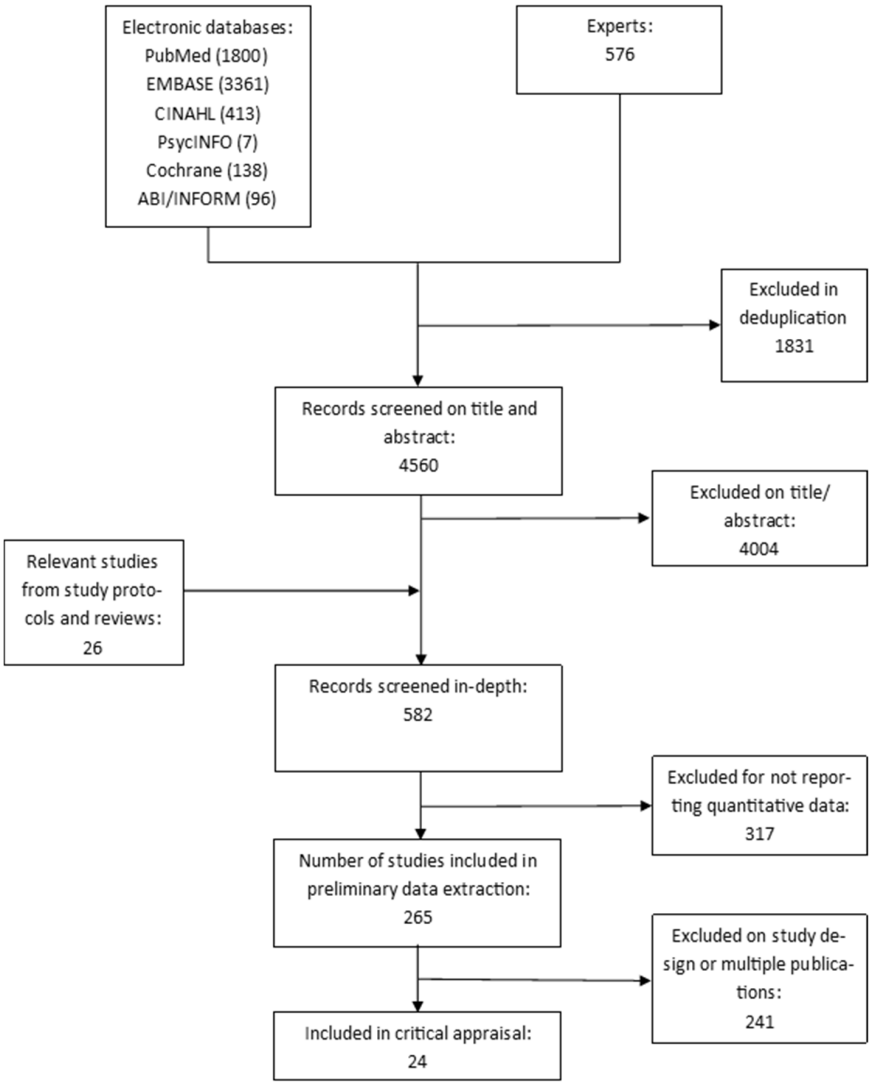

Figure 2 Flow chart of the study selection process.

RISK OF BIAS ASSESSMENT

Most studies had a high risk of bias because of not reporting baseline characteristics (n=12), inadequate allocation concealment (n=9) or no random sequence generation

(n=8); the majority of these studies were performed with a controlled before-after design. Only 2 studies reported the number of missing values and how they were handled, while the other 22 studies did not. In addition, baseline characteristics were most often only described of the hospitals and/or patients, but characteristics of the care providers on which the interventions were focused (e.g. physicians) were rarely reported. All but one study (Karagounis et al, interpretation of electrocardiograms [13]) used objective outcome measures. The results of the risk of bias assessments are presented in Figure 2.

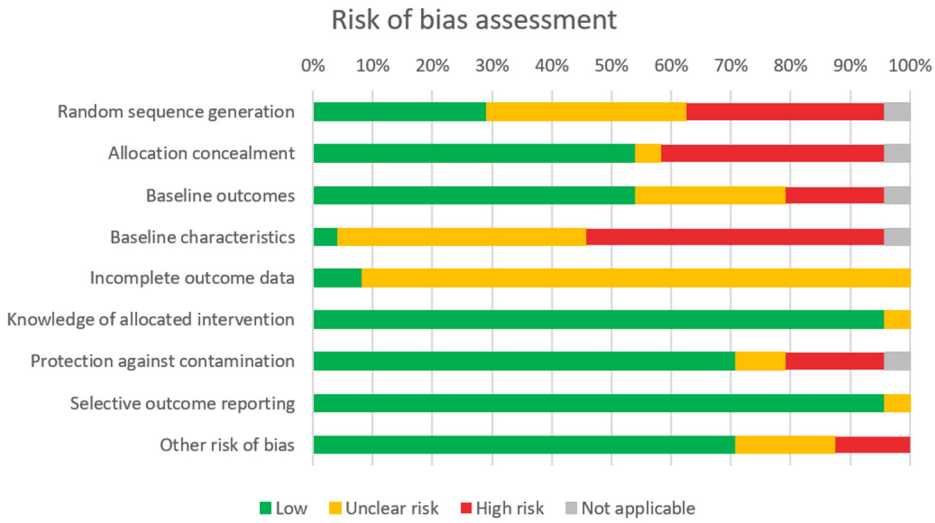

Figure 3 Results of the risk of bias assessment of all included studies (n=24) according to the suggested EPOC risk of bias criteria.

INTERVENTION COMPONENTS

In total, 23 different intervention components were identified in the studies. The component *audit & feedback* was most often used (12 studies)[14-25], followed by *educational interventions* (11 studies)[16-20, 23, 26-30], *educational materials* (7 studies)[16, 26, 28-32] and *local opinion leaders* (6 studies)[15, 19, 20, 27, 30, 32]. The other 19 intervention components were applied in fewer than 4 studies. Five studies had an intervention of 1 component, 3 studies had 2 components and the other 16 studies had an intervention with ≥3 components. The median number of components per study was 3, ranging from 1 to 6. The intervention components are summarized in Table 4.

Table 4 An overview of the included studies and their intervention components

First author	# of components (categorization)	Components	Average effect*
Bailey	6 (complex)	Use of information and communication technology, role expansion, monitoring performance, academic detailing, inter-professional education, reminders	+3%
Beck	1 (simple)	Audit & feedback	-2%
Berner	3 (complex)	Monitoring the performance of delivery, audit & feedback, local opinion leaders	+1%
Berwanger	4 (complex)	Reminders, continuity of care, educational materials, educational meetings	+6%
Brush	4 (complex)	Reminders, audit & feedback, educational materials, educational meetings	+1%
Carlhed	4 (complex)	Audit & feedback, educational meetings, multidisciplinary teams, continuous quality improvement	+14%
Du	3 (complex)	Audit & feedback, educational meetings, local consensus processes	+6%
Ellerbeck	2 (simple)	Audit & feedback, continuous quality improvement	+3%
Flather	5 (complex)	Local opinion leaders, educational meetings, educational materials, academic detailing, continuous quality improvement	+4%
Glickman	1 (simple)	Pay for performance	+3%
Gomez	3 (complex)	Role expansion, educational materials, site of service delivery	N/A
Goodnough	4 (complex)	Reminders, educational meetings, educational materials, local consensus processes	N/A
Heller	3 (complex)	Audit & feedback, local opinion leaders, educational meetings	N/A
Karagounis	1 (simple)	Telemedicine	N/A
Kinsman	4 (complex)	Audit & feedback, local opinion leaders, educational meetings, care pathways	-14%
Loten	1 (simple)	Integration of services	+11%
Mehta	4 (complex)	Academic detailing, local opinion leaders, educational materials, local consensus processes	+7%
Peacock	1 (simple)	Accreditation	0
Renzi	2 (simple)	Audit & feedback, public release of performance data	+2%
Robinson	2 (simple)	Audit & feedback, continuous quality improvement	+23%
Romero	3 (complex)	Educational meetings, educational materials, local consensus processes	+5%
Sauaia	2 (simple)	Audit & feedback, educational meetings	-2%
Soumerai	3 (complex)	Local opinion leaders, educational meetings, educational materials	+6%
Tu	3 (complex)	Audit & feedback, public release of performance data, tailored interventions	+2%

* The average effect was calculated by averaging the difference in performance between intervention and control groups. Studies in grey included fewer than 1000 patients. N/A = no relevant outcomes reported as % in the study.

PROCESS MEASURES

In the studies, the following measures were subjected to improvement interventions: the number of pharmaceutical prescriptions, time to diagnosis, time to medication, time to PCI, referral to a smoking cessation program, risk assessment, risk stratification, use of diagnostics, referral to cardiac rehabilitation, referral to dietary counselling, length of hospital stay, number of blood transfusions, cholesterol measurement, and use of quality improvement tools. Of the 24 studies, only two studies included patient outcomes in addition to process outcomes.[14, 18] Negative indicators, i.e. a process that should not be initiated when it is not required (e.g. because a superior alternative is available, it has no value or its effectiveness has been disproved), were reported in two studies (use of lidocaine[30] and use of thrombolysis in patients without a confirmed myocardial infarction[22]). Few studies reported the actual number of patients who were eligible for a process measure and what the performance was (e.g. the total number of patients without contraindications that received a beta blocker on admission).

SYNTHESIS

Most studies only reported the performance in percentages without reporting measures of variance/spread such as standard deviations or confidence intervals, rendering it impossible to calculate pooled effect sizes and confidence intervals. Consequently, the overall effects of the interventions were estimated by only calculating the performance in percentages and ranges between studies. Four studies could not be included in the synthesis since their outcomes were continuous instead of dichotomous.[13, 19, 28, 31] In addition, six studies were considered small and were therefore not included in calculating the average effects. [20, 22, 23, 29, 33, 34]

The average performance improved 3.8%, ranging from a deterioration of 3% to an improvement of 14%. In Figure 3, the comparison between studies with simple (≤2 components) or more complex (≥3 components) is presented. For the larger studies, the average percentage improvement in performance was 0.6% (range: -3% to +3%) for the simple interventions and 5.6% (range: +2% to +14%) for the more complex interventions.

ID	Performance intervention	Performance control	Difference
Robinson 1996	84	61	+23
Loten 2010	71	60	+11
Sauaia 2000	75	76	-1
Beck 2005	71	74	-3
Peacock 2013	90	91	-1
Glickman 2007	81	78	+3
Renzi 2012	29	27	+2
Ellerbeck 2000*	60	58	+2
Kinsman 2012	62	76	-14
Bailey 2007	94	91	+3
Romero 2005	61	56	+5
Berwanger 2012	85	79	+6
Mehta 2002	80	74	+6
Berner 2003	65	63	+2
Flather 20111	84	80	+4
Du 2014	62	56	+6
Carlhed 2006	79	65	+14
Tu 2009	75	72	+3
Brush 2009	97	94	+3
Soumerai 1998*	87	81	+6

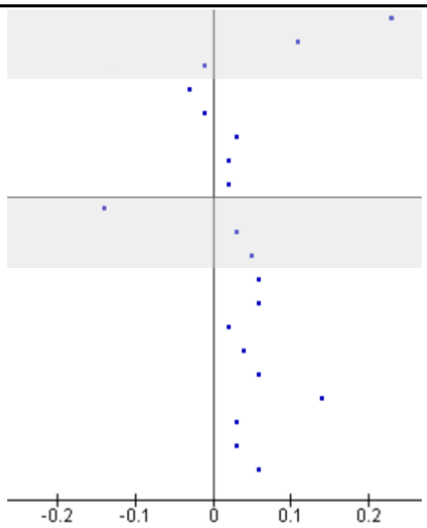

Figure 4 Comparison of the total change in performance between simple (top part of the figure) and more complex (bottom part of the figure) interventions. The studies are arranged on the number of patients included from least to most; studies in the grey areas included fewer than 1000 patients. In studies with an * the total number of patients was not reported, but the number of included hospitals was high enough to assume inclusion of more than 1000 patients.

In the Figures 3-6, the results of the most common intervention components are displayed. For audit and feedback, the interventions with audit and feedback as a component resulted in an average improvement of 3.6% (range: -3% to 14%). For educational meetings, the total intervention resulted in an average improvement of 6.5% (range: +3 to +14%). Interventions with educational materials as a component resulted in an average improvement of 5% (range: +3 to +6%). For local opinion leaders, the average improvement was 4.5% (range: +2 to +6%).

ID	Performance intervention	Performance control	Difference
Kinsman 2012	62	76	-14
Robinson 1996	84	61	+23
Sauaia 2000	75	76	-1
Berner 2003	65	63	+2
Du 2014	62	56	+6
Beck 2005	71	74	-3
Carlhed 2006	79	65	+14
Tu 2009	75	72	+3
Brush 2009	97	94	+3
Renzi 2012	29	27	+2
Ellerbeck 2000	60	58	+2

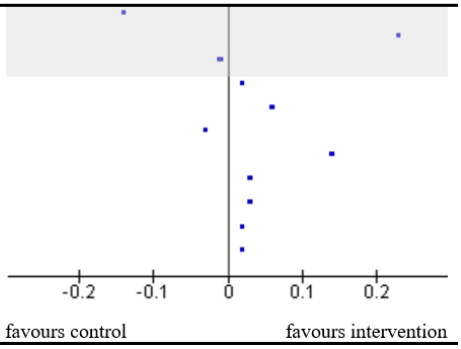

Figure 5 Overview of interventions with audit and feedback as a component. Studies in the grey areas included fewer than 1000 patients. After the study ID, the performance in the intervention group, performance in the control group and the difference are presented.

ID	Performance intervention	Performance control	Difference
Kinsman 2012	62	76	-14
Romero 2005	64	56	+5
Sauaia 2000	75	76	-1
Berwanger	85	79	+6
Flather 2011	84	80	+4
Du 2014	62	56	+6
Carlhed 2006	79	65	+14
Brush 2009	97	94	+3
Soumerai 1998	87	81	+6

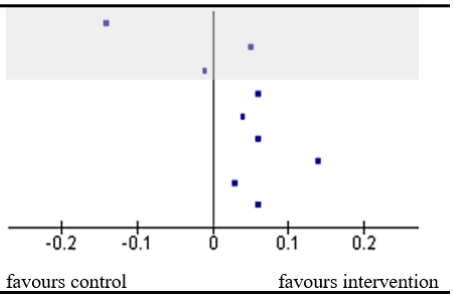

Figure 6 Overview of interventions with educational meetings as a component. Studies in the grey areas included fewer than 1000 patients. After the study ID, the performance in the intervention group, performance in the control group and the difference are presented.

ID	Performance intervention	Performance control	Difference
Romero 2005	64	56	+5
Berwanger	85	79	+6
Mehta 2002	80	74	+6
Brush 2009	97	94	+3
Soumerai 1998	87	81	+6

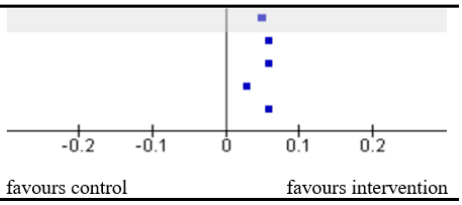

Figure 7 Overview of interventions with educational materials as a component. Studies in the grey areas included fewer than 1000 patients. After the study ID, the performance in the intervention group, performance in the control group and the difference are presented.

ID	Performance intervention	Performance control	Difference
Kinsman 2012	62	76	-14
Mehta 2002	80	74	+6
Berner 2003	65	63	+2
Flather 2011	84	80	+4
Soumerai 1998	87	81	+6

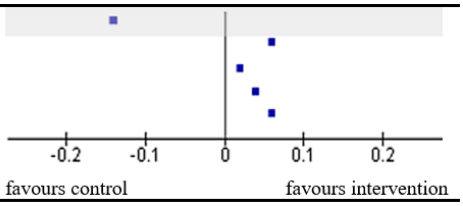

Figure 8 Overview of studies with interventions with local opinion leaders as a component. Studies in the grey areas included fewer than 1000 patients. After the study ID, the performance in the intervention group, performance in the control group and the difference are presented.

DISCUSSION

In this systematic review, an overview of interventions to improve the process of care for patients with acute coronary syndrome was provided. The majority of the studies focused on improving pharmacological prescriptions and were single centre, non-controlled before-after studies. After including only the studies with the strongest designs, most studies showed that interventions were overall modestly effective in improving guideline adherence. More complex interventions appeared more effective in improving performance than simpler interventions.

Although most interventions resulted in improvement, the differences between the interventions were large. The majority of interventions consisted of multiple components, however only four EPOC intervention components were identified more than four times. There is a nearly infinite number of combinations of these elements to design an intervention. After excluding smaller studies, the largest improvement was achieved in a setting where a national ACS care register was used to measure performance and facilitate targeted quality improvement. In the study, multidisciplinary teams of cardiologists and nurses were trained in continuous quality improvement in accordance with the breakthrough method.[35] Additional papers have been published on the study, describing the intervention and follow-up results in more detail.[8, 36, 37] One precondition for such an intervention is a fully operational national cardiology registry, which emphasizes the value of such a registry as the foundation for quality management.

In this systematic review, the overall effectiveness of interventions containing similar components was calculated. Interventions with audit and feedback appears to have a small positive effect on the process measures, thereby confirming findings of other

studies.[38] Several aspects facilitate the effectiveness of audit and feedback: a low pre-intervention performance; interdisciplinary provision; a higher frequency, both verbal and written feedback; and inclusion of clear targets and action plans.[38] Other intervention components also resulted in small improvements, which confirms the findings of other reviews on reminders [39, 40], local opinion leaders [41], printed educational materials [42] and educational meetings [43].

The study designs identified in the overview of studies (n=265) generally resulted in a low level of evidence. The majority of the studies were single centre, non-controlled before-after studies. After selecting only the studies with the strongest research designs, high risks of bias were regularly identified. The baseline characteristics of neither care providers nor patients were reported in many studies, thereby limiting external validity. In addition, authors often did not report how missing data were handled or did not make (report the) use of a random sequence generation. In several studies, the data analyses were not corrected for clustering of patients within centres, which can lead to spurious significant results.[44] It appeared that smaller studies reported more extreme results (either positive or negative) than larger studies.

All studies included in this review reported the performance on process measures for eligible patients, i.e. implementation. However, only two studies also reported negative measures, i.e. measuring the number of patients not eligible for a process measure who do receive it.[22, 30] Although implementation research is important to distribute effective interventions, there appears little attention for de-implementation of obsolete interventions, or for appropriate use. In studies on e.g. the prescription of beta blockers, usually only the number of eligible patients (without contraindications) receiving them is reported. In contrast, the number of patients with contraindications that do receive them can be informative from a patient safety perspective.

IMPLICATIONS FOR PRACTICE

Many different interventions can be used for improving process measures. In this study, multifaceted interventions appeared more effective in improving practice than single interventions. It can be recommended to combine several intervention components in order to achieve a larger improvement in performance. It is not known what the most effective combination of components is and whether there is an optimal combination of intervention components. However, combining intervention components with specific purposes (e.g. providing an overview of current performance, organizing educational

meetings and materials to initiate change, and continuing efforts to ensure change) is highly recommended. It is paramount that the performance is not only measured, but feedback is provided and there is a system to use targeted quality improvement efforts, sufficiently supported by the care providers. In addition, to limit the administrative burden, only the most essential variables should be recorded.

Implementation research has taught us that the attitude of care providers affects their likelihood to adopt an intervention. Lack of knowledge of, and a negative attitude towards guideline recommendations have been identified as the most important barriers in guideline adherence.[45] Despite this large impact on implementation, the attitude of care providers towards the process measures was only reported in one study.[29] Interventions such as educational meetings, educational materials and local opinion leaders are predominantly aimed at affecting the attitude and can therefore be important when improving guideline adherence.

IMPLICATIONS FOR RESEARCH

In this study, the quality of reporting of studies was frequently inadequate. This has been identified as an issue in a previous systematic review of interventions to improve care for patients with diabetes mellitus type II.[46] Reporting of complex interventions is frequently inadequate for policy makers to translate into practice. As a result, reporting criteria for complex interventions (StaRI [47]) and quality improvement efforts (SQUIRE [48]) can be of great benefit to the quality of reporting quality improvement efforts. In addition, the EPOC framework can be used to report the different components of the intervention.[11]

Adequate reporting is not only important for composition of the intervention and the setting in which it is applied, but also for its delivery. In this review, we found that only few studies reported information on compliance of interventions. In one of the studies included in this systematic review, it is reported that only 13 of the 19 hospitals held the planned educational sessions for hospital staff, while 6 did not.[19] Reporting the delivery of the intervention is advocated in all studies on complex interventions [49] and can be a valuable addition in health services research. For policy makers and quality officers, it is vital to assess whether an intervention could work in their setting. Through collecting data on the process of implementation by means of document analyses, stakeholder interviews, observations and/or monitoring of routine data, the process of implementation can be evaluated (process evaluation).[50] In the report, the

authors should describe what the intervention entailed, how it was implemented, and what the mechanisms of impact were.

LIMITATIONS

The results of this study should be considered in the light of some limitations. First, although full meta-analyses (with a pooled effect sizes and corresponding confidence intervals) are the preferred form of knowledge synthesis, this could not be performed in this study. Most studies did not report the number of eligible patients per process measure, thereby rendering the calculation of confidence intervals impossible. The calculation of the average effects and corresponding ranges of the comparisons in this review (simple vs complex and the four intervention components) are crude measures and should therefore be interpreted with caution. Second, there were large differences in the settings, interventions, outcomes and number of outcomes per study, making comparison between interventions difficult. In this review, the aim of our study was to provide an overview of the interventions used in cardiology, and therefore we decided to include all interventions aimed at improving guideline adherence in ACS care. It is not known whether these studies can be repeated with similar results in other settings. Fourth, although a taxonomy was used for characterizing the interventions, within the categories there is ample room for variation. For example, feedback of performance can vary in the person or institution providing the feedback, the delivery method (digitally, on paper, in person) and the frequency of feedback. Also, different interventions components can be combined, making it unclear what the contribution of a single component is. The average effects should therefore be interpreted with caution. Finally, in the calculation of the improvement per study, the performance on multiple process measures was compared between the intervention and control groups of the studies. These results do not take potential baseline differences in the measures or variation into account.

CONCLUSION

Many studies have attempted to improve the process of ACS care, especially the prescription of medication and to reduce the time to PCI. However, the study designs generally resulted in a low level of evidence. In studies with stronger research designs, audit & feedback, educational materials and meetings, and local opinion leaders were the most common interventions. Improvement of performance was reported in the majority of studies, no matter what intervention(s) was/were used. Combining multiple intervention components appeared more effective than one or two

components. Quality in reporting was poor however, and recent reporting guidelines on complex interventions and quality improvement can be of great value to the field of implementation research and ACS care.

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DISCLOSURES

None.

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Chapter 8

Discussion and reflection

Although the quality of care for patients with ACS has improved tremendously over the years, the burden of this disease is still high.[1] To further improve the quality of care and consequently patient outcomes, European clinical guidelines have been released. However, the implementation of these guidelines appears to be suboptimal in Dutch hospitals,[2] potentially resulting in unwarranted practice variation and suboptimal patient outcomes. To improve guideline adherence in ACS care, a quality improvement program was developed. This program consisted of, among other things, multiple quality indicators and a national online tool where the hospitals could upload their results on the quality indicators.[3] However, the proposed online tool was terminated prematurely. Consequently, the information about the quality of ACS care in Dutch hospitals is scarce.

To fill this gap, the quality of ACS hospital management was evaluated by measuring multiple process quality indicators, as presented in the previous chapters of this thesis. The research questions of the research presented in this thesis were:

1) to what degree are the guideline recommendations for minimizing treatment delay in STEMI and the prescription of secondary prevention medication in ACS adhered to in Dutch hospitals?

2) to what extent is there unwarranted process variation in the performance of hospitals on these quality indicators?

3) what interventions are effective for improving the ACS care process?

In this chapter, the main findings of the studies are synthesized per research question; the VMS ACS quality indicators are reflected upon; (methodological) considerations about the research are presented and recommendations for clinical practice and future research are made.

1) To what degree are the guideline recommendations for minimizing treatment delay in STEMI and the prescription of secondary prevention medication in ACS adhered to in Dutch hospitals?

Because no reliable national data on ACS management were available, these were collected in a cross-sectional study (chapter 2). This study was designed to measure guideline adherence for treatment delay in STEMI; use of risk scoring tools in NSTEMI and UA (results presented in the thesis of Engel[4]); and prescription of secondary

prevention medication in all ACS patients. In total, 13 hospitals participated in this study. The results are discussed per indicator.

GUIDELINE ADHERENCE: TREATMENT DELAY

Seven of the 13 hospitals provided primary PCI. Of the 1017 STEMI patients going for primary PCI, 800 (78.7%) were treated within the recommended maximal treatment delay of 90 minutes. The median treatment delay was 64 minutes (interquartile range: 47-82 minutes) (chapter 3).

The median treatment delay in our study appeared shorter than as reported in a recent Dutch publication: 64 minutes versus 75 minutes (interquartile range: 51-108 minutes).[5] The data for this publication was collected by a Dutch data registry during four 'snapshot weeks'. In these weeks, several hospitals reported multiple performance indicators to the data registry. Potential explanations for the difference between the results are differences in the patient population (e.g. more patients with acute heart failure / cardiogenic shock) and the method of data collection.

Although room for improvement was identified in our study, the overall performance in Dutch hospitals was high in comparison to studies performed abroad. The median delay in studies performed abroad was 86-90 minutes.[6-8] However, several factors impede direct comparison of these results to results of studies performed abroad: the small land area of the Netherlands and the relatively high number of PCI centres; the distinctive health care system (with an important role for general practitioners); the developed emergency medical services system with prehospital ECGs; and the use of different definitions of treatment delay. In countries similar to the Netherlands in some factors (e.g. other countries with a small total land area and highly developed emergency medical services such as Denmark), similar short treatment delays were reported.[9] In the Danish study, the treatment delay was defined as ranging from the call to the emergency medical services to PCI. Despite this broader definition, the median delay was 75 minutes (for patients living within 10 km of a PCI centre). However, Denmark has more centralized PCI services, with only four centres performing primary PCI[10] instead of the 30 centres in the Netherlands. Their median delay was higher for patients living further from a PCI centre: a median delay of 134 minutes for patients living >100 km from a PCI centre.[9] In contrast, in the Netherlands no, or very few, patients live >100 km from a primary PCI centre, with consequently shorter driving times and treatment delays. Nevertheless, the research presented in this thesis shows areas for improvement in acute STEMI management in the Netherlands.

GUIDELINE ADHERENCE: SECONDARY PREVENTION MEDICATION

The guideline adherence for prescribing secondary prevention medication at discharge from the hospital was substantial. Of the 2471 patients with ACS, 1708 (69.1%) were treated according to the guidelines. This performance was comparable to the results of a regional study performed in the Netherlands, in which 65.2% of the patients were discharged with the recommended secondary prevention medication.[11] The percentage of guideline adherence in our study varied between medications, from 76.8% for the ACE inhibitor to 99.6% for acetylsalicylic acid.

Although the performance in studies performed abroad showed a similar picture, some differences occur. For example, in a large European study (the Euro Heart Survey), the average percentages of discharge medication ranged from 66% for thienopyridines to 99.6% for the acetylsalicylic acid in STEMI patients, and from 59% for thienopyridines (a subgroup of p2Y12 inhibitors) to 88% for aspirin in NSTE-ACS patients.[12] Consequently, the performance as measured in our study was relatively high. This might be caused by the fact that individual patient records were screened and potential contra-indications were retrieved from all records. Not including contra-indications, the performance on guideline adherence in our study was 49.1% for all five medications, ranging from 64.9% for the ACE inhibitor to 92.8% for the statin. In contrast, a recent publication about a study performed in the United Kingdom reported guideline adherence as high as ranging from 89.3% for P2Y12 inhibitor to 98.7% for aspirin.[13] Therefore, the guideline adherence appears to have improved over the years and further improvement in the Netherlands appears feasible.

2) To what extent is there unwarranted process variation in the performance of hospitals on these quality indicators?

PROCESS VARIATION: TREATMENT DELAY

Despite a short median treatment delay, we identified several non-medical factors associated with a longer treatment delay, indicating unwarranted process variation. These factors were similar to the ones identified in previous international studies[7, 14]: requiring inter-hospital transfer and presentation with acute heart failure (chapter 3). However, these studies also identified presentation during off-hours and co-morbidity such as diabetes and chronic heart failure as predictors of time delays, while this was not the case in our study. The difference in presentation during off-hours can be explained by potential differences in the after-hours care between the study settings. For example, due to the small country size of the Netherlands in comparison to the United States, the majority of interventional cardiologists and catheterization room

nurses live near the hospital and can arrive at the hospital within 20 minutes of being called. In contrast, in the United States, only 10.7% hospitals expected their staff to arrive within 20 minutes.[15]

In a qualitative study, numerous differences in the processes from first electrocardiogram to PCI were identified between PCI centres. In addition, accelerating factors were identified and the results were synthesized in a model (chapter 5). The most important differences between the centres were: the profession of the care coordinator; communication of diagnostic information (transmittal of ECGs); making the decision to initiate catheterization; catheterization room preparation; and accommodation of the patient in case the catheterization room is occupied. Different choices in maintaining the balance between speed and accuracy of the diagnosis, as well as situational differences (e.g. the presence of residents), resulted in differences in the processes. Furthermore, several factors were identified by care providers as influencing the speed of the process. These factors could be categorized as patient characteristics (e.g. clear signs and symptoms); healthcare providers characteristics (e.g. experience), inter-provider characteristics (e.g. clear communication); and hospital characteristics (e.g. anticipating variations in patient routing). Both the variation in the process as well as the factors influencing the speed of the process were summarized in a model, which can be used by PCI centres to reflect upon their acute care process and to identify the factors that can be improved.

PROCESS VARIATION: SECONDARY PREVENTION MEDICATION

Considerable variation between hospitals and patient groups was identified in the prescription of secondary prevention medication after ACS (chapter 6). While in the most compliant hospital the guidelines were adhered to in 87% of the patients, this was only 42.1% in the least compliant hospital. These differences could not be explained by differences in the patient populations. Furthermore, several patient groups were identified that received secondary prevention medication less often according to the guidelines. These were patients with NSTEMI or UA (compared to patients with STEMI); patients with a history of CABG; and elderly women. A potential explanation for the suboptimal prescription of secondary prevention medication could be the limited hospital length of stay. With a median length of stay of five days, there is little room for establishing the optimal dosage, in particular for the blood pressure lowering medication in elderly women.

Internationally, differences between hospitals in the prescription of secondary prevention medication for ACS patients have also been identified. For example, in a

study performed in Sweden and the UK, the prescription of statin at discharge from the hospitals was 87.2% (interquartile range for hospitals: 81.4-91.3%) and 94.3% (interquartile range for hospitals: 90.7-96.9%) respectively.[13] For the ACE inhibitor/ angiotensin II receptor inhibitor (AIIRB) this was 63.6% (interquartile range for hospitals: 57.1-69.8%) and 84.9% (interquartile range for hospitals: 79.7-90.5%) respectively. In addition to differences between hospitals, these results also show large differences between countries. In a European study, the guideline adherence for the ACE inhibitor ranged from 61% in Spain to 90% in the Czech Republic. In the Netherlands and Belgium, the guideline adherence ranged between 68% for the ACE inhibitor to 92% for the dual anti-platelet (acetylsalicylic acid and clopidogrel, a P2Y12 inhibitor).[16] Direct comparison between the results of this study and our study is difficult, however. Many differences in definitions were identified. For example, there were differences in the patient groups (e.g. ACS, STEMI, NSTEMI, NSTE-ACS), the medications (e.g. clopidogrel, thienopyridine, P2Y12 inhibitor, dual antiplatelet therapy), timing (at discharge, after 30 days) or how contra-indications were handled (not taking contra-indications into account, only including patients without contra-indications, defining contra-indications per medication). Consequently, comparisons between studies should be interpreted with caution.

These variations in both treatment delay and the prescription of secondary prevention medication indicate that, despite an overall fair performance, differences in processes and performance occur between countries, between hospitals and between patient groups. These differences indicate room for improvement in the quality of the process of care for patients with ACS in Dutch hospitals.

3) What interventions are effective for improving the ACS care process?

One of the reasons to choose ACS as a subject for the VMS quality improvement program was that several interventions to improve the care process were previously described in scientific literature. However, these interventions had never been systematically assessed on their effectiveness in ACS management. In our systematic review, we showed that studies evaluating these interventions often had an inadequate research design. From the studies with the strongest research designs, we learned that audit & feedback, educational interventions, educational materials and local opinion leaders were the most often used intervention components. The interventions were aimed at improving e.g. pharmaceutical prescriptions; time to diagnosis; time to PCI; referral to a smoking cessation program; and use of risk stratification. The majority

of the interventions were modestly effective in improving guideline adherence. The findings in our systematic review confirm the findings of several Cochrane reviews. In these reviews, single components of interventions were evaluated, e.g. audit and feedback[17], reminders[18, 19], local opinion leaders[20] printed educational materials[21] and educational meetings[22]. In all these systematic reviews, the authors concluded that the intervention had small to modest effects on improving professional practice. In addition, the results of our systematic review showed that interventions consisting of multiple components were more effective in improving the process of ACS care than interventions with one or two components. To further improve the process of care for patients with ACS, multicomponent interventions (e.g. a combination of feedback of performance, training of care providers in continuous quality improvement and use of local opinion leaders) are therefore recommended (chapter 7).

REFLECTION

REFLECTION ON THE VMS QUALITY INDICATORS

Development and measurement of quality indicators is a time- and resource-intensive process.[23] Although many quality indicators are measured by all Dutch hospitals[24], not all quality indicators provide relevant information for the stakeholders. Several criteria can be used to separate useful quality indicators from indicators that predominantly contribute to an administrative burden. According to the study of Campbell *et al*[25], a useful indicator should be:

- acceptable to stakeholders;
- feasible (e.g. data availability);
- reliable (e.g. minimal measurement error);
- sensitive to change;
- predict patient outcomes (predictive validity).

It is of vital importance to keep these criteria in mind when developing quality indicators. Additionally, these criteria can be used to evaluate and improve current quality indicators, such as the VMS ACS quality indicators.

Although the evaluation research on the VMS program concluded that a broad movement in patient safety had been initiated and the program should be continued,[26] several opportunities for improving the VMS ACS indicators can be identified in retrospect by applying the criteria of Campbell *et al.*.

Acceptable to stakeholders:
Both the VMS ACS indicators and their evaluation received considerable criticism from cardiologists.[27, 28] This criticism potentially points out a lack of support for, and/or priority of the subject. This might have contributed to the lack of data entry in the online VMS tool. A potential reason for the lack of support and/or priority is that although the VMS ACS care guide states that the quality indicators were based on the ESC guidelines, they deviate from these guidelines on multiple aspects (for examples, see chapters 3, 4 and 6). The Netherlands Society of Cardiology (NVVC) decided to endorse the ESC guidelines as the foundation for Dutch ACS care. An exception is the 2015 guideline on the management of ACS patients without persistent ST-segment elevation[29], which was not endorsed for, among other reasons, the bleeding risk of triple antithrombotic therapy (i.e. aspirin, P2Y12 inhibitor and (non-vitamin K) oral anticoagulation). Separate recommendations for the care of this patient group were published in an NVVC working group statement.[30] The current VMS quality indicator for secondary prevention medication deviates from the ESC guidelines and working group statement (published after the development of the quality indicators) on several aspects. For example, the strong recommendations (level of evidence 1A) for prescribing an ACE-inhibitor and a beta-blocker in the ESC guideline only apply to patients with heart failure or left ventricular dysfunction. In contrast, the VMS quality indicator makes no distinction. In addition, the quality indicators as described in the ESC guidelines only apply to the care for patients with STEMI and NSTEMI, while the VMS indicators also include patients with UA.[31] Recently, a working group of the Acute Cardiovascular Care Association (ACCA) published a position paper on the use of quality indicators in evaluating STEMI and NSTEMI management.[32] In re-evaluating the definitions and in- and exclusion criteria of the Dutch quality indicators, it is recommendable to stay as close to the endorsed European guidelines and working group statements as possible.

Feasible:
In most hospitals, the data required for reporting the quality indicators was only available in the patient records. This meant that a tremendous effort would be required of hospital personnel to retrieve the available data. In addition, not all relevant time points were available in the hospital information systems, forcing hospitals to initiate labour- and time-intensive manual data extraction. This might have been another factor in the lack of data delivery to the prematurely terminated online VMS tool. In future quality indicator development, either data availability should play a more influential role in the selection of the indicators, or hospitals should be assisted in data

retrieval. Pilot testing of the indicators can lead to tremendous improvements before implementation on a national level. For example, many hospitals had no straightforward procedure to retrospectively select patients with ACS. During these pilot tests, a uniform procedure for selecting the patients with ACS eligible for the quality indicators could have been described. Pilot testing can also be used for finetuning the definitions and in- and exclusion criteria of the indicators, and thereby contribute to the selection of comparable patient groups in all hospitals.

Reliable:
The reliability of both the treatment delay and secondary prevention medication indicators can be further improved by re-evaluating their definitions and in- and exclusion criteria. For example, the starting point of the treatment delay indicator was defined as the time of first (para)medical contact. However, it was not defined whether this concerns physical contact or e.g. calling the national emergency number. This led to the use of different definitions between hospitals, thereby hampering the reproducibility as well as the comparability of the results between hospitals. For secondary prevention medication, developing clear in- and exclusion criteria (taking into account contra-indications) is strongly recommended. These in- and exclusion criteria can be based on the codebooks developed for our studies (chapter 2).
Quality indicator developers in the Netherlands can learn from the AHA/ACC quality indicators[33], which are developed using a template with clear definitions for e.g. a numerator, denominator, period of assessment, data source, rationale and corresponding guideline recommendations. The recent ESC Acute Cardiovascular Care Association (ACCA) working group position paper can also be used as an example for improving the definitions.[32]

Sensitive to change:
In our systematic review (chapter 7), several studies were included with similar quality indicators, i.e. treatment delay and prescription of medication. Many of these studies showed improvements in indictor scores after quality improvement programs were initiated. Therefore, the quality indicators appear sensitive to change.

Predictive validity:
Both treatment delay and secondary prevention medication are correlated with mortality in studies with ACS patients and therefore these quality indicators fulfil this criterium.[34, 35]

(METHODOLOGICAL) CONSIDERATIONS

The results presented in this thesis need to be interpreted in the light of several considerations.

CROSS-SECTIONAL DESIGN

The studies presented in this thesis were performed in a cross-sectional design. Two important assumptions were made: 1) that the performance of hospitals is (to some extent) consistent over time, and 2) that the random selection of hospitals was representative for all Dutch hospitals. When these assumptions are met, random samples from the time period can be extrapolated to the entire time period, i.e. the year 2012, and from the selected hospitals to all hospitals in the country. However, the measurements were performed during the VMS quality improvement program, which might have led to improved performance over the year. By adding the measurement times to the statistical models as a covariate, potential influences of the measurement times on the results can be identified. No significant influences were identified in these models, which indicate no or limited influence of the measurement times on the performance. Since not all hospitals agreed to participate in the study, there is a risk of selection bias, in that only the hospitals motivated for quality measurement participated. However, the number of hospitals that declined participation was small. Also, different types of hospitals did participate (academic, PCI hospital and non-PCI hospital, teaching and non-teaching), which enhances the generalizability of the results of our studies. We therefore assume that potential effects on the outcomes of our studies are limited.

In our cross-sectional study, data were only collected on the hospital management and a minor part of prehospital management of ACS. However, multiple health care providers play a role in ACS management, i.e. from control of risk factors at the general practitioner to the acute care at the hospital, rehabilitation and eventually the long-term check-ups with the cardiologist and general practitioner for secondary prevention. In addition, several other elements such as patient outcomes and successfully performed PCI or CABG are (at least) equally important in the quality of hospital care for patients with ACS. Consequently, no conclusions can be drawn about the overall quality of ACS management in the Netherlands.

STRUCTURE, PROCESS AND OUTCOME

The final goal of all quality improvement efforts should be to improve the patient outcomes. Measuring processes is not a substitute for measuring outcomes, but it does

provide us with the insights to improve the process, in order to improve outcomes.[36] The works of Donabedian were based on the idea that process improvements should eventually lead to improvements in patient outcomes. However, establishing the link between process and outcome is challenging. In the management of ACS, several studies have been able to establish this link. For example, the study of Peterson *et al.* showed that improvements in the process of ACS management in Sweden correlated with improvements in outcomes.[35] The results of other studies agree that there appears a correlation between the quality as measured by processes and outcomes[13, 37, 38], although there is no definitive answer yet.[39] In contrast, the study of Menees *et al.* showed that an average reduction of 16 minutes in the door-to-balloon times did not result in reduced mortality for patients with STEMI in a large data registry.[40] This study highlights the importance of critically evaluating the association of process measures and patient outcomes. Although measuring process measures can contribute to an effective quality improvement system, it should always be the means to an end.

MISSING DATA

The retrospective nature of the data collection in the patient record review studies (chapters 2, 3 and 6) has several important implications. The results of this type of study are dependent on the quality of the data documented at the hospitals. It is challenging to assess the quality of this data retrospectively. For example, missing information can have multiple causes: the information was not obtained (e.g. no past medical history of the patient was obtained prior to an emergency PCI procedure); the information was not documented (e.g. a past medical history was obtained but not documented in the patient record); or there was nothing to report (e.g. the patient had no relevant past medical history). Identifying the cause of the missing data is difficult, thereby impeding the choice between for example 'not documented/missing' or 'no medical history' on the case report form. This might have affected the results of the patient record review studies. However, no major differences between the multiple chart reviewers were identified in the inter-reviewer measurements, indicating that the information was interpreted similarly by different chart reviewers. The most common situations with missing data were documented in a codebook for the chart reviewers. This codebook was updated regularly, as is considered good practice in patient record review.[41] In addition, when the information was considered not to be obtained or not documented, appropriate data imputation techniques were used, depending on the pattern of missingness.[42] Exclusion of patients with incomplete data would result in discarding valuable information that was collected for these patients. In addition, it has

the potential to introduce bias when the patients with incomplete data differ from the patients with complete data. Multiple imputation was required for treatment delay, as there were associations between the chance of missingness in one variable and the value of another variable.[42] As these associations were absent in the secondary prevention medication data, single imputation was sufficient. The results of all analyses on these imputed data sets incorporate an uncertainty about the imputed data, resulting in larger confidence intervals. We therefore expect limited influence on the direction or size of the results.

APPROPRIATE USE CRITERIA

The focus on guideline adherence in this thesis is limited to identifying adherence with positive recommendations of the guidelines: evaluating whether patients who are eligible for a certain intervention also receive it, i.e. appropriate use. Another side of guideline adherence is evaluating whether patients who are not eligible for a certain clinical intervention do receive that intervention, i.e. inappropriate use. For example, one of the recommendations in the European Society of Cardiology guidelines is that a PCI of a totally occluded artery >24h after symptom onset in stable patients without signs of ischaemia is not recommended. For these patients, the PCI procedure offers no or very little benefit, while it does have the potential to harm. It is possible to identify patients with a totally occluded artery >24h after symptom onset and measure how many of these patients underwent PCI. In the systematic review on interventions to improve guideline adherence, only two studies reported such measures (chapter 7). A tool for dealing with such issues is to identify *appropriate use criteria*, for example for revascularization.[43] The method of appropriate use criteria involves the presentation of clinical scenarios which were developed to mimic patient presentations encountered in everyday practice. These scenarios are scored by a panel of experts on whether revascularization is appropriate, uncertain or inappropriate. This approach facilitates monitoring of processes, both for appropriate use and inappropriate use.

Internationally, there has been much attention for these 'negative' recommendations. In the United Kingdom, the National Institute for Clinical Excellence (NICE) has developed a 'do-not-do' list, in which clinical practice that should be discontinued or not used routinely is described.[44] This has been translated to the Dutch setting in the '*beter niet doen*' list.[45] In future practice, these 'negative' recommendations can be considered for the development of quality indicators.

RECOMMENDATIONS FOR CLINICAL PRACTICE AND FUTURE RESEARCH

From the results of the research presented in this thesis, several recommendations can be made for clinical practice and future research.

MAINTAIN THE BALANCE BETWEEN SPEED AND DIAGNOSTIC ACCURACY

An optimal balance between speed of the process and diagnostic accuracy should be identified for patients with STEMI referred for emergency PCI. This balance should minimize both the treatment delay and the number of false catheterization room activations. The balance is also influenced by the strength of the association between treatment delay and the risk of dying. When the association is strong,[46] then the balance will swing more to prioritizing speed. When the association is weaker,[40] the balance will swing more to prioritizing the accuracy of the diagnosis, resulting in fewer inappropriate catheterizations. Use of computer simulation allows for manipulation of multiple variables at once and can therefore be used to determine an optimal balance.

Although many patients arrive through the emergency medical services, the longest delays were identified in patients arriving through alternative routes. In countries such as the United States, where the majority of treatment delay research was performed, more patients arrive through the emergency department.[37] Therefore, multiple interventions to decrease treatment delay at the emergency department have been developed, which might be applicable to the Dutch emergency departments. For patients arriving through the emergency department of both PCI centres and non-PCI centres, rapid rule out protocols can play an important role in keeping the treatment delay short. Also, activation of the catheterization laboratory by emergency physicians can be useful in reducing the treatment delay.[47]

In addition, improving cooperation between all stakeholders in the region of a PCI centre has the potential to reduce the treatment delay. In both our study and international studies[7], arriving through a non-PCI hospital was the strongest predictor of a longer treatment delay. Therefore, efforts to improve cooperation should focus on health care providers working in the alternative patient routes, i.e. emergency physicians, cardiologists at non-PCI hospitals, general practitioners and care providers working at non-cardiac hospital departments. This should result in shared protocols with not only the emergency medical services, but also general practitioners, emergency departments, other hospital departments and referring hospitals.[48]

REDUCE VARIATION IN THE PRESCRIPTION OF SECONDARY PREVENTION MEDICATION

To improve the quality of secondary prevention, cardiologists should be aware of their leading role in the prescription of secondary prevention medication and referral to cardiac rehabilitation. From a study in Denmark, we learned that patients who are not prescribed the recommended medication at discharge from the hospital are unlikely to ever receive it in their entire post-hospital care trajectory.[49] Prescribing this medication at discharge from the hospital or during a follow-up visit is therefore essential in maintaining the continuum of care.[50] In case the short length of hospital stay after an ACS leaves too little time to initiate the medication adequately, clear instructions for the patient's primary care provider on prescribing secondary prevention medication are vital.

Although large differences between hospitals in prescribing the secondary prevention medication at discharge were identified in our study, the data offers no insight in the causes of these differences. For example, the data were inadequate to identify differences between cardiologists. Therefore, in-depth research is needed, both quantitative (e.g. differences between individual cardiologists/residents/nurse specialists) and qualitative (e.g. the differences in culture between departments).

To improve the prescription of secondary prevention medication, there are tools that use potential differences between individuals as the foundation for quality improvement. One commonly used tool in the Netherlands is the medical audit: a systematic evaluation of guideline adherence, most often performed in the preparation for a peer quality review. In a medical audit, cardiologists working within a department evaluate each other's records of patients with ACS on guideline adherence and collectively identify targets for improvement. This offers cardiologists the possibility to learn from one another and improve the overall quality of care provided at their department. Consequently, a medical audit should be developed for ACS care in the Netherlands including secondary prevention, based on the ESC guidelines and the NVVC and ACCA position papers.

IMPROVE INFORMATION SYSTEMS

Before the quality of care can be measured uniformly between hospitals, much improvement is required in the information systems of hospitals. In the process of acute care for patients with STEMI, much of the required information was lacking, resulting in difficulties in measuring performance on quality indicators. Hospitals varied greatly in the extent to which they documented the different time variables, resulting in large

differences in quality indicator performances (chapter 4). While some hospitals had almost complete data about the entire care pathway of patients in one database, others relied on multiple freestanding databases that were difficult to link on a patient level.
One of the most important improvements that can enable uniform measurements between hospitals and facilitate future quality improvement is the formation of a national cardiology data registry in which all hospitals participate.[27] Examples of these databases can be found all over Europe, including the UK (MINAP)[51] and Sweden (SWEDEHEART)[52]. These registries can facilitate improvement in guideline adherence, sharing of best practices and monitoring of patient outcomes over time. Setting up a widely used registry has proven to be difficult, deeming by Dutch initiatives such as the Dutch *National Cardiology Data Registry* (NCDR), *Begeleidingscommissie Hartinterventies Nederland* (BHN) and *Meetbaar Beter*. Each of these registries focusses on a specific part of cardiology services: NCDR on devices and interventions, BHN on interventions, and Meetbaar Beter on patient outcomes (but not processes). These multiple initiatives have led to an incomplete and fragmented view of the quality of cardiology services in Dutch hospitals. Each approach has its advantages and disadvantages. For example, an outcome based approach incorporates what eventually matters (improved patient outcomes), but many outcomes are relatively rare, making it difficult to identify differences between hospitals.[53] In case clinically relevant differences are found and processes were not measured, it is unclear how these improved patient outcomes were achieved. Consequently, structure and process indicators can contribute to further quality improvement in an outcome-based approach.
Recently, the chairmen of the boards of the three Dutch data registries have signed a letter of intent for integrating their registries into one: the Netherlands Heart Registry. Combining the registries should result in a more integrated insight in both cardiology structures, processes and patient outcomes. An additional benefit is that combining three registries into one results in uniform definitions and a reduction of the administrative burden. In integrating multiple registries into a national registry, experiences from other countries (e.g. Sweden)[54, 55], or other medical conditions (e.g. stroke)[56] can be used to facilitate optimal use of the registry as the foundation for quality improvement at hospitals.
One hiatus in the current registries is cardiac rehabilitation. In a previous report, it is demonstrated that the cardiac rehabilitation programmes offered in hospitals can be improved.[26] For example, not all cardiology departments had written agreements with cardiac rehabilitation providers. Therefore, cardiac rehabilitation should be included in the Netherlands Heart Registry.

The data in the Netherlands Heart Registry should be validated at least periodically and/or by other means of sampling. In the cross-sectional studies presented in this thesis, a sample of the patient records was screened by two raters independently and differences were identified. Although the overall agreement was good, the double screening of records resulted in some improvements in the data, but even more so in the definitions in the codebooks. In addition, the data were entered in a data entry program with fixed entry fields using different data types (e.g. date, time, binary, category) and were compared to the original case report form by a second researcher. Finally, the data were checked for impossible combinations, e.g. a negative treatment delay, and outliers, e.g. ages >100 years. All these steps improved the quality of the data used for the analyses performed as part our research, and should also be considered for the Netherlands Heart Registry, as is already the case in the Meetbaar Beter program.

LIMIT THE ADMINISTRATIVE BURDEN

In Dutch health care, the role of quality indicators has been growing in the last decades. In addition to multiple health care quality indicators (e.g. Dutch Healthcare Inspectorate indicators, Zichtbare Zorg, VMS), indicators about e.g. the quality management system, continued education, fire safety and finances are also obligatory. Although digitalization of hospitals' information systems facilitated data management and retrieval, retrieving the right information to calculate these indicators still puts an incredible burden on health care organizations. This requires a significant investment of hospitals in software and personnel for administrative support, data management and quality management.[57] The number of measures and the number of data items per measure will always be a balance between informational needs on the one hand and administrative burden on the other. By spending more time on administration, resources are used that could have been employed for patient care. However, when the information is used in a correct way, it might lead to a return on investment, i.e. the improvement that can be made based on the quality information is larger than the care that could have been provided by e.g. hiring an additional nurse. Therefore, it is recommended to only measure aspects of quality which are likely to be used for quality improvement and/or accountability. Primarily, the focus should be on performance measures with a proven relationship with quality (e.g. the number of PCI procedures per operator[58]). Consequently, current quality indicators with a questionable or no relation to quality should be considered for abandonment. Since the ultimate goal of quality indicators is to improve care, indicators with a lack of support from care providers, or with little or no variation in performance or room for improvement have little added

value.[25] From the field of general practice, we have learned that quality indicators can be withdrawn without negative consequences for the quality of care.[59]
Another way to limit the administrative burden is uniformization of data and data requirements. Ideally, the information in patient records recorded by care providers is recorded once and can subsequently be used for multiple purposes, e.g. patient care, quality improvement, communication with other care providers and accountability. However, the documentation and especially the possibilities for data extraction have been suboptimal so far, hampering the use of this information for other purposes than patient care. Consequently, the Netherlands Federation of University Medical Centres in cooperation with Nictiz (centre of expertise for standardisation and eHealth) initiated the program *'Registratie aan de bron'*.[60] The goals of this program are to improve the quality, re-use and interoperability of the documented information in hospitals; to optimize the care processes; and to demonstrate improved patient outcomes. By streamlining the information requirements of multiple stakeholders, the program should alleviate the administrative burden of health care providers while improving the quality of the documentation of medical information.[24] Only when relevant high quality data can be generated without intensive manual labour is (real-time) comparison of performance on quality indicators between hospitals feasible.

FACILITATE CONTINUOUS QUALITY IMPROVEMENT

While the information presented in this thesis can be used to target quality improvement efforts in the Dutch cardiology care, current use of quality information by health care providers for quality improvement is limited.[57] In our systematic review, the most effective intervention for improving ACS care from a reliable study was based on the use of quality information in national registry combined with training of care providers in continuous quality improvement, i.e. targeted quality improvement.[61] It should be clear that providing feedback of performance alone is not enough to stimulate quality improvement. National organizations of cardiologists and nurses working in cardiology should offer training to care providers in targeted quality improvement. This training should focus on how can you use the results of quality indicators, national registries and/or local databases to further improve the quality of care. However, this is only possible when the administrative burden is diminished and the time saved is attributed to targeted quality improvement.

RESEARCH DEPARTMENT COMPETENCIES AND SUSTAINABILITY OF QUALITY IMPROVEMENT

The differences in prescription of secondary prevention medication between hospitals could not be explained by hospital characteristics. However, they might be related to characteristics of departments or teams. For the education of future physicians, a framework was developed for competencies of individual physicians: the CanMEDS framework. However, a department of competent individuals does not automatically make it a competent department. It is unclear what characteristics of departments or teams are related to guideline adherence and a high quality of care. In chapter 7, interventions were identified that promote guideline adherence. However, it is unknown whether these interventions are equally effective in all departments and teams, or that characteristics of these departments or teams determine the effectiveness of these interventions to some extent. It would therefore be recommendable to research characteristics of departments or teams that are associated with guideline adherence and effective use of quality improvement interventions. These characteristics could be used to create a framework of for department competencies.

In addition, if departments are able to improve the quality of care, it is essential to sustain that improvement. Several context factors that contribute to sustainability have been identified in past research,[62] however long-term effects have not been researched. Recommendations for research would therefore be: 1) to identify characteristics of high quality departments in order to create a framework of department competencies; and 2) identify effective interventions for sustaining quality improvement.

IMPROVE GUIDELINE DEVELOPMENT AND ADAPTATION IN CARDIOLOGY

In the management of ACS in hospitals, the NVVC is responsible for the development and distribution of clinical guidelines. The NVVC has opted for endorsing several ESC guidelines, thereby agreeing that these guidelines are the foundation for the treatment of patients with ACS in the Netherlands. However, the development of the ESC guidelines does not appear to adhere to the current quality standards for the development of evidence-based guidelines.[63] For example, there is no description of the clinical questions that the guidelines should answer; the literature searches and seeking patients' views and preferences are not described in the methods; and the criteria for selecting the evidence are missing. Without adhering to these quality criteria, the guideline development process is insufficiently transparent. This lack of transparency can result in a diminished support for the guideline recommendations and less successful implementation.[64-66] A European effort is required in order to improve the cardiology guideline development, of which the NVVC can be the instigator.

In addition, the translation of international guidelines to a national setting is difficult. Therefore, the Guidelines International Network (GIN) developed a toolkit to adapt guidelines from other settings (ADAPTE).[3] Use of this toolkit should result in improved translation of the international guideline recommendations (including the performance indicators) to the Dutch setting and thereby improving guideline adherence and eventually patient outcomes.

CONCLUSION

In conclusion, although the performance of hospitals on the VMS quality indicators for treatment delay and secondary prevention medication is fair, there is still room for improvement. PCI centres can learn from one another about how to design and execute an efficient care process for patients with STEMI, in consultation with other involved care providers (e.g. ambulance services, non-PCI hospitals and emergency departments). Also, there is unwarranted variation between hospitals in the prescription of secondary prevention medication at discharge. The VMS ACS quality indicators may have contributed to improving ACS care to some extent, however there are several possibilities for improving them. Further quality improvement in ACS care can be facilitated by synthesizing the information in current ACS quality registries into the Netherlands Heart Registry, facilitating continuous quality improvement, and initiating multicomponent quality improvement interventions based on the results of the Netherlands Heart Registry. Further research is required on the balance between speed and diagnostic accuracy; the cause of variation in the prescription of secondary prevention medication; a framework of department competencies and the sustainability of quality improvement. Finally, a European effort is required to improve the development of the ESC guidelines and their translation to the Dutch setting.

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Summary
Samenvatting
Dankwoord

SUMMARY

INTRODUCTION

Acute coronary syndrome (ACS) is the most common ischaemic heart disease and one of the leading causes of death in the world. Although improvements in the quality of care have led to tremendous improvements in patient outcomes, the burden of the disease is still high. Three clinical manifestations can be distinguished: ST-segment elevation myocardial infarction (STEMI); non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina (UA). The management of these three clinical manifestations differs on some aspects. In the acute management of STEMI, it is vital that patients are treated with percutaneous coronary intervention (PCI) as soon as possible, as the likelihood of dying after STEMI increases with time. All patients with an ACS have an increased risk of a recurring ACS. Therefore, they receive several medications for secondary prevention: acetylsalicylic acid, P2Y12 inhibitor, statin, beta blocker and an Angiotensin converting enzyme (ACE)-inhibitor.

In the Netherlands, the Dutch Society of Cardiology (NVVC) has adopted the European Society of Cardiology guidelines as the foundation for the management of ACS patients. In general, adhering to these guidelines can be considered good quality of care, although the physicians can always deviate from the guidelines with sound medical rationale. However, the guideline adherence is often suboptimal. To measure the guideline adherence, the most important recommendations of guidelines can be translated into quality indicators.

Following a critical report on the quality of Dutch care, a national quality improvement program (VMS) was initiated in 2008, in which ACS management was one theme. Within this VMS program, five quality indicators were developed for the management of patients with ACS. In this thesis, two of these indicators with an established association with patient outcomes were evaluated: use of PCI within 90 minutes of first medical contact for patients with STEMI; and the prescription of secondary prevention medication at discharge from the hospital for all patients with ACS. For these two indicators: 1) the performance in Dutch hospitals was measured; 2) (unwarranted) process variation was investigated in-depth; and 3) effective interventions to further improve the care processes were identified.

METHODS AND RESULTS

Because no reliable national data on ACS management was available, a cross-sectional study was designed to measure guideline adherence in hospitals using the VMS ACS quality indicators **(Chapter 2)**. In total, 13 hospitals selected by means of a multistage random selection procedure participated in the study, of which seven provided PCI. The data were extracted from the patient records. In addition to data on guideline adherence, data on several patient and hospital characteristics were collected in order to identify (unwarranted) practice variation. Missing data were handled with the appropriate (multiple) imputation procedures. The data were analysed with generalized linear (mixed) models.

TREATMENT DELAY

In total, 1017 records of patients with STEMI going for immediate PCI were included in the study. The majority (78.7%) were treated within the recommended 90 minutes. The median treatment delay was 64 minutes (interquartile range: 47 – 82 minutes). Significantly prolonged treatment delays were found in patients of whom their first electrocardiogram was performed at the general practitioner's practice or at the hospital; who required interhospital transfer; or who presented with acute heart failure **(Chapter 3).** Large differences in the quality of the data impeded comparison of the treatment delay between the PCI centres. In addition, different definitions of treatment delay are used internationally, hampering comparison of our results to the results of studies performed abroad **(Chapter 4).** To investigate the acute STEMI care process in-depth, a qualitative study was performed in six of the seven PCI centres. At each hospital, involved care providers were interviewed, resulting in 28 interviews. For each centre, the acute care process was mapped and compared to the guideline recommended care process and to the processes of other PCI centres. The processes in the centres differed from the guideline recommended process on e.g. additional (unavoidable) patient routings such as patients coming through the general practitioner, and no continuous monitoring of the treatment delay. The processes in the centres differed from one another in the communication of diagnostic information (e.g. transmitting all, only ambiguous or no electrocardiograms) and catheterization room preparation. These differences indicate that in hospitals different choices are made to maintain a balance between speed and diagnostic accuracy. Factors perceived by care providers as accelerating the process included trust in the tentative (prehospital) diagnosis, and avoiding unnecessary inter-caregiver consultations. The differences in the processes and the accelerating factors were summarized in a model, which can be used in other PCI centres to critically reflect on their own STEMI care process **(Chapter 5).**

SECONDARY PREVENTION MEDICATION

In total, 2471 records of patients discharged with an ACS were included in the study. Guideline adherence was defined as prescription of all five recommended medications at discharge from the hospital or documentation of a contra-indication or other reason for not prescribing them. Complete guideline adherence was achieved in 69.1% of the patients. However, this ranged from 42.1% to 87.0% between hospitals. The ACE inhibitor was most often missing (21.2%). Guideline adherence was less often achieved patients with NSTEMI or UA; patients with a history of coronary artery bypass grafting or elderly women. Because the overall performance was substantial, quality improvement efforts can be targeted at underperforming hospitals and undertreated patient groups. **(Chapter 6)**

QUALITY IMPROVEMENT

In order improve the guideline adherence in the hospital care of patients with ACS, a systematic review was performed to identify effective quality improvement interventions for optimizing the ACS care processes. In this systematic review, an overview was provided of 265 papers on initiatives aimed at improving the ACS care process. The most often reported subjects for improvement were medication prescription; treatment delay, and referral to smoking cessation. However, the findings of the majority of these studies were insufficiently reliable. Consequently, the 24 studies with the strongest research designs were selected for further investigation. Using the Cochrane Effective Practice and Organisation of Care (EPOC) taxonomy of health systems interventions, 23 different intervention components were identified. The most commonly used intervention components were audit & feedback; educational interventions; educational materials; and local opinion leaders. In the majority of the studies, the interventions were (to some extent) effective in improving guideline adherence. Interventions consisting of multiple components (e.g. a combination of feedback of performance, training of care providers in continuous quality improvement and use of local opinion leaders) appeared more effective than single or dual component interventions. **(Chapter 7)**

REFLECTION, (METHODOLOGICAL) CONSIDERATIONS AND RECOMMENDATIONS

Although the performance of hospitals on the VMS quality indicators for treatment delay and secondary prevention medication was fair, there was unwarranted practice variation. Although the VMS program has initiated a broad movement in patient safety,

several opportunities for improving the VMS ACS indicators could be identified in retrospect **(Chapter 8)**. Especially the acceptability to the stakeholders, feasibility (e.g. required data) and reliability (e.g. definitions and in- and exclusion criteria) require further attention in case the use of these indicators is continued.

The results of the research presented this thesis should be interpreted in the light of several considerations. First, the guideline adherence was measured using cross-sectional studies performed in hospitals and not in the entire ACS care pathway. Second, only processes were measured in the research presented in this thesis, not structures or outcomes. However, measuring processes offers the most practical information for quality improvement and therefore were the focus of this thesis. Third, due to the retrospective nature of these studies, the percentage of missing data was high. Therefore, we had to use appropriate statistical techniques to correct for this. Fourth, by measuring the VMS ACS quality indicators, we only evaluated whether patients who were eligible for an intervention also received it. In contrast, we did not evaluate whether patients who were not eligible for an intervention did receive it (appropriate use). The recent initiative of the '*beter niet doen*' list shows that some of these 'negative' recommendations can be considered for the development of quality indicators.

From the research presented in this thesis, several recommendations can be made for clinical practice and future research**:**

- **Maintain the balance between speed and diagnostic accuracy**

Although the median treatment delay was relatively short in comparison to studies abroad, the recommended maximal treatment delay of 90 minutes was exceeded occasionally. To further improve care processes, hospitals can learn from one another about how to design the acute care process for patients with STEMI. They can focus on patients presenting through other routings than the emergency medical services. The model presented in **Chapter 5** can be helpful in this. Although further speeding up the process can be important, it is vital to maintain the balance between speed of the process and diagnostic accuracy. Consequently, both the treatment delay and the number of unnecessary catheterization room activations should be monitored in hospitals.

- **Reduce variation in the prescription of secondary prevention medication**

Although the prescription of secondary prevention medication was largely in accordance with the guidelines, there was much unwarranted variation among hospitals and among different patient groups. Cardiologists should be aware of their leading role in initiating secondary prevention medication in the entire care pathway. Further research is needed on the causes of the large differences between hospitals and potentially between cardiologists. By making use of the interventions recommended in **Chapter 7** of this thesis, unwarranted practice variation can be reduced and the quality of care further improved. Besides these interventions, ACS management including secondary prevention medication can be a subject for the medical audits as used in the Dutch system of peer quality review.

- **Improve information systems**

Currently, there are several national data registries of the management of ACS that have different visions in monitoring and improving the quality of care. By combining these efforts, comparable to the Swedish SWEDEHEART model, the current fragmented view of the quality of ACS management in the Netherlands can be improved and the administrative burden reduced to some extent. It is essential to follow-up on the letter-of-intent to integrate the current data registries into the Netherlands Heart Registry. In a national registry, data validation is essential for the quality of the data and consequently the reliability of the results.

- **Limit the administrative burden**

An opportunity for alleviating the administrative burden is to abandon quality indicators which show no or limited room for improvement. To efficiently use the available data, care providing institutions should employ the time gained by abandoning quality indicators for using results of relevant quality indicators and registries for targeted quality improvement efforts. Another way to limit the administrative burden is standardization of data and data requirements, e.g. through the *'Registratie aan de bron'* initiative.

- **Facilitate continuous quality improvement**

The results of our systematic review showed that only providing feedback of performance is not enough to stimulate quality improvement. The largest improvements were achieved by a combination of feedback of performance and training in continuous

quality improvement, i.e. targeted quality improvement. Therefore, national organizations of cardiologists and nurses working in cardiology could offer training to care providers in targeted quality improvement.

- **Research department competencies and sustainability of quality improvement**

A department of good individuals does not make a good department. Therefore, identifying a framework for high performance departments can be of added value. In addition, if quality improvement is achieved, it needs to be sustained. Consequently, the sustainability of quality improvement should be further researched.

- **Improve guideline development and adaptation in cardiology**

Finally, the VMS ACS quality indicators were based on the European Society of Cardiology guidelines for STEMI and for NSTEMI & UA management. However, the development of these guidelines does not adhere completely to the current quality standards for guideline development. In addition, because the Dutch Society of Cardiology adopts these guidelines, there is room for improvement in the adoption and adaptation process.

SAMENVATTING

INTRODUCTIE

Acuut coronair syndroom (ACS) is de meest voorkomende ischemische hartziekte en één van de belangrijkste oorzaken van vroegtijdige sterfte in de wereld. Ondanks dat veranderingen in de zorg hebben geleid tot grote verbeteringen in uitkomsten voor patiënten en een betere kwaliteit van zorg, is de ziektelast nog steeds hoog. ACS is te onderscheiden in drie klinische manifestaties: ST-segment elevatie hartinfarct (STEMI); niet-ST-segment elevatie hartinfarct (NSTEMI) en instabiele angina pectoris (IAP). De behandeling van deze drie klinische manifestaties verschilt op enkele onderdelen. In de acute behandeling van STEMI is het essentieel dat ze zo snel mogelijk gedotterd worden, omdat de kans op overlijden toeneemt naarmate de tijd verstrijkt. Alle patiënten die een ACS hebben doorgemaakt hebben een verhoogd risico op nog een ACS. Daarvoor krijgen ze secundaire preventie medicatie: acetylsalicylzuur, P2Y12-remmer, statine, bètablokker en een angiotensine converterend enzym (ACE) remmer.

In Nederland heeft de Nederlandse Vereniging voor Cardiologie (NVVC) de Europese richtlijnen geadopteerd als basis van de behandeling van patiënten met een ACS. Het handelen conform deze richtlijnen wordt in het algemeen gezien als goede zorg, hoewel afwijken van de richtlijnen om medische redenen altijd mogelijk is. Echter, de implementatie van de richtlijnen is vaak suboptimaal. Om de implementatie te meten worden de belangrijkste aanbevelingen uit de richtlijnen vertaald in kwaliteitsindicatoren.

In navolging van een kritisch rapport over de kwaliteit van de Nederlandse zorg werd een nationaal kwaliteitsverbeterprogramma opgezet (VMS), waarvan ACS één van de thema's was. Binnen dit thema werden vijf kwaliteitsindicatoren ontwikkeld. In dit proefschrift zijn de twee kwaliteitsindicatoren geëvalueerd die een bewezen associatie met patiëntuitkomsten hebben: het dotteren binnen 90 minuten na eerste (para) medisch contact voor patiënten met STEMI, en het voorschrijven van secundaire preventie medicatie bij ontslag uit het ziekenhuis voor alle patiënten met ACS. Voor deze twee indicatoren: 1) zijn de prestaties van Nederlandse ziekenhuizen gemeten; 2) is de variatie in de processen onderzocht; en 3) zijn interventies voor het verbeteren van de zorgprocessen geïdentificeerd.

METHODEN EN RESULTATEN

Omdat betrouwbare landelijke data niet beschikbaar waren, is een dwarsdoorsnedestudie opgezet om het volgen van de richtlijnen te meten middels de VMS ACS indicatoren. **(Hoofdstuk 2)** In totaal werden met een procedure voor gestratificeerde willekeurige selectie 13 ziekenhuizen geselecteerd voor deelname, waarvan zeven ziekenhuizen dotterbehandelingen uitvoerden. De data werden verzameld uit patiëntendossiers. In aanvulling op informatie over het volgen van de richtlijnen werd tevens informatie over patiënt- en ziekenhuiskarakteristieken verzameld om (onnodige) praktijkvariatie te kunnen onderzoeken. Voor ontbrekende data werden gepaste (meervoudige) imputatieprocedures gebruikt. De data werden vervolgens geanalyseerd door middel van generaliseerde lineaire (mixed) modellen.

TIJD TOT DOTTERBEHANDELING

In totaal werden 1017 dossiers van patiënten met STEMI die een acute dotterbehandeling kregen geïncludeerd in de studie. Het overgrote deel (78,7%) werd binnen de aanbevolen 90 minuten gedotterd. De mediane tijd tot dotterbehandeling was 64 minuten (interkwartielafstand: 47 – 82 minuten). Een significant langere tijd tot behandeling werd gevonden bij patiënten van wie het eerste elektrocardiogram gemaakt werd bij de huisarts of in het ziekenhuis, patiënten die van het ene ziekenhuis naar het andere vervoerd moesten worden, en patiënten die zich presenteerden met acuut hartfalen **(Hoofdstuk 3).** Door grote verschillen in de kwaliteit van de data was de tijd tot behandeling moeilijk te vergelijken tussen de dottercentra. Tevens werden internationaal andere definities gehanteerd voor tijd tot dotterbehandeling, waardoor onze resultaten moeilijk te vergelijken zijn met resultaten uit buitenlandse studies **(Hoofdstuk 4).** Om het acute STEMI zorgproces nader te onderzoeken, werd een kwalitatieve studie uitgevoerd in zes van de zeven dottercentra. In totaal werden 28 interviews afgenomen met de belangrijkste betrokkenen in het zorgproces van ieder ziekenhuis. Van ieder dottercentrum werd het acute zorgproces in kaart gebracht en vergeleken met het proces zoals aanbevolen in de richtlijnen en met elkaar. De processen in de dottercentra verschilden van het proces zoals aanbevolen in de richtlijnen op, onder andere, het hebben van aanvullende (onvermijdelijke) patiëntstromen zoals patiënten die via de huisarts komen, en het niet continu monitoren van de tijd tot dotterbehandeling. De processen in de centra verschilden van elkaar in de communicatie van diagnostische informatie (bijvoorbeeld het doorsturen van alle, alleen onduidelijke/dubieuze, of geen elektrocardiogrammen), en het voorbereiden van de hartcatheterisatiekamer. Deze verschillen tonen aan dat in ziekenhuizen verschillende keuzes worden gemaakt

in het waarborgen van een balans tussen snelheid en accuratesse van de diagnose. Zorgverleners ervoeren vertrouwen in de voorlopige (prehospitale) diagnose en het vermijden van onnodige consultaties tussen zorgverleners als versnellende factoren. De resultaten van de variatie in de processen en de versnellende factoren zijn samengevoegd in een model wat gebruikt kan worden in andere dottercentra om op hun eigen acute zorgproces te reflecteren **(Hoofdstuk 5).**

SECUNDAIRE PREVENTIE MEDICATIE

In totaal werden 2471 patiëntendossiers van patiënten ontslagen met een ACS geïncludeerd in de studie. Het handelen conform de richtlijnen was gedefinieerd als het voorschrijven van alle vijf de aanbevolen medicijnen of het documenteren van een contra-indicatie of andere reden voor het niet voorschrijven van de medicijnen. De richtlijnen werden volledig gevolgd bij 69,1% van de patiënten. Echter, dit varieerde van 42,1% tot 87,0% tussen ziekenhuizen. De ACE-remmer ontbrak het vaakst (21,2%). De richtlijnen werden minder vaak gevolgd bij patiënten met NSTEMI of IAP; patiënten met een openhartoperatie in de voorgeschiedenis; en oudere vrouwen. Omdat de resultaten in het algemeen ruim voldoende waren, kunnen kwaliteitsverbeteringen gericht worden ingezet bij minder goed presterende ziekenhuizen en onderbehandelde patiëntgroepen. **(Hoofdstuk 6)**

KWALITEITSVERBETERING

Om het volgen van de richtlijnen in de ziekenhuiszorg voor patiënten met ACS te verbeteren, is een systematisch literatuuronderzoek uitgevoerd om effectieve interventies te identificeren. In dit systematische literatuuronderzoek werd een overzicht gegeven van 265 artikelen over kwaliteitsverbeterinitiatieven rondom het ACS zorgproces uit de wetenschappelijke literatuur. De meest voorkomende onderwerpen voor verbetering waren het voorschrijven van medicatie; de tijd tot dotterbehandeling of trombolyse en verwijzen naar stoppen met roken programma's. Echter, de resultaten van het merendeel van deze studies waren onvoldoende betrouwbaar. Daarom zijn de 24 studies met de sterkste onderzoeksdesigns geselecteerd voor nader onderzoek. Met het *Cochrane Effective Practice and Organisation of Care* (EPOC) classificatie van interventies binnen zorgsystemen werden 23 verschillende interventie componenten onderscheiden. De meest voorkomende componenten waren audit & feedback, onderwijsinterventies, onderwijsmaterialen en lokale opinieleiders. Het merendeel van de onderzochte interventies zorgden er (tot op zekere hoogte) voor dat richtlijnen beter gevolgd werden. Interventies die bestonden uit meerdere componenten

(bijvoorbeeld een combinatie van het meten en terugkoppelen van prestaties, trainen van zorgverleners in continue kwaliteitsverbetering en het inzetten van lokale opinieleiders) leken een groter effect te hebben dan interventies bestaande uit één of twee componenten. **(Hoofdstuk 7)**

REFLECTIE, (METHODOLOGISCHE) OVERWEGINGEN EN AANBEVELINGEN

Hoewel de VMS programma heeft gezorgd voor een brede beweging in patiëntveiligheid, zijn er verschillende mogelijkheden om de ACS indicatoren van het programma te verbeteren (Hoofdstuk 8). Met name de onderwerpen *acceptatie door betrokkenen*, *haalbaarheid* (bv. de benodigde data) en *betrouwbaarheid* (bv. de definities en in- en exclusiecriteria) vereisen aandacht wanneer de indicatoren gebruikt blijven worden.

De resultaten van het onderzoek uit dit proefschrift moeten worden geïnterpreteerd in het licht van enkele (methodologische) overwegingen. Ten eerste, het volgen van de richtlijnen is gemeten door middel van een dwarsdoorsnede onderzoek in ziekenhuizen en daarmee niet in het volledige ACS zorgproces. Ten tweede zijn in het onderzoek zoals gepresenteerd in dit proefschrift alleen processen gemeten, geen structuren of uitkomsten. Echter, het meten van processen biedt de meeste aangrijpingspunten voor kwaliteitsverbetering en was daarom het onderwerp van dit proefschrift. Ten derde, vanwege de retrospectieve aard van het onderzoek was het percentage ontbrekende data hoog. Daarom hebben we passende statistische technieken moeten gebruiken om hiervoor te corrigeren. Ten vierde, door het meten van de VMS ACS kwaliteitsindicatoren hebben we alleen onderzocht of patiënten die in aanmerking kwamen voor een interventie deze ook kregen. Daarentegen hebben we niet onderzocht of patiënten die niet in aanmerking kwamen deze interventie toch ontvingen (gepast gebruik).

Uit het onderzoek gepresenteerd in dit proefschrift, kunnen verschillende conclusies en aanbevelingen voor de praktijk en onderzoek worden gehaald**.**

- **Waarborg de balans tussen snelheid en diagnostische accuratesse**

Ondanks dat de mediane tijd tot dotterbehandeling relatief kort was in vergelijking met studies uit andere landen, werd de maximale tijd tot dotterbehandeling nog af en toe overschreden. Om de zorgprocessen verder te verbeteren kunnen ziekenhuizen veel van elkaar leren over hoe het acute zorgproces voor patiënten met STEMI ingericht kan worden. Het model zoals gepresenteerd in **Hoofdstuk 5** kan ziekenhuizen helpen hierbij. Hoewel het verder versnellen van het proces belangrijk kan zijn in het

terugdringen van de sterfte aan STEMI, is het essentieel om de balans tussen snelheid van het proces en de zorgvuldigheid omtrent het stellen van de diagnose goed te bewaken. Daarom dient men in ziekenhuizen zowel de tijd tot dotterbehandeling als het aantal keren dat de hartcatheterisatiekamer onnodig geactiveerd wordt te monitoren.

- **Reduceer de variatie in het voorschrijven van secundaire preventie medicatie**

Hoewel secundaire preventie medicatie grotendeels conform de richtlijnen werd voorgeschreven, was er veel onnodige variatie in de prestaties tussen ziekenhuizen en tussen patiëntgroepen. Cardiologen dienen zich bewust te zijn van hun leidende rol in het initiëren van secundaire preventie medicatie in het hele zorgproces. Meer onderzoek is nodig naar de redenen van de grote variatie tussen ziekenhuizen en mogelijk tussen cardiologen. Door de interventies te gebruiken zoals beschreven in **Hoofdstuk 7** van dit proefschrift, kan onnodige praktijkvariatie worden verminderd. Aanvullend hierop kan secundaire preventie medicatie onderwerp worden van de '*medical audits*', zoals worden uitgevoerd in het Nederlandse systeem van de kwaliteitsvisitaties.

- **Verbeter de informatiesystemen**

In de huidige situatie bestaan er verschillende landelijke kwaliteitsregistraties die verschillende visies hebben op het monitoren en verbeteren van de kwaliteit van ACS zorg. Door de verschillende registraties te combineren, vergelijkbaar met het Zweedse *SWEDEHEART* model, kan de huidige, gefragmenteerde monitoring verbeteren en de administratieve last enigszins worden beperkt. Het is essentieel dat er een vervolg wordt gegeven aan de recent getekende intentieverklaring om de drie bestaande dataregistraties samen te voegen in de Nederlandse Hart Registratie. In een landelijke registratie is het essentieel dat de data gevalideerd worden. Dit komt de kwaliteit van de data en de betrouwbaarheid van de resultaten ten goede.

- **Verminder de administratieve last**

Een mogelijkheid voor het verlichten van de administratieve last is om kwaliteitsindicatoren die geen, of een beperkte, ruimte voor verbetering laten zien te schrappen. Om de beschikbare gegevens beter te benutten, dienen zorgverlenende instellingen de gewonnen tijd door het schrappen van indicatoren in te zetten om de resultaten van relevante kwaliteitsindicatoren en kwaliteitsregistraties te gebruiken voor gerichte kwaliteitsverbetering. Een andere mogelijkheid om de administratieve last te reduceren is standaardisatie van data en data vereisten, bijvoorbeeld in het 'Registratie aan de bron' programma.

- **Faciliteer continue kwaliteitsverbetering**

De resultaten van ons systematische literatuuronderzoek tonen aan dat alleen het terugkoppelen van prestaties onvoldoende is om kwaliteitsverbetering te stimuleren. De grootste verbeteringen werden behaald door een combinatie van het terugkoppelen van prestaties en het trainen in continue kwaliteitsverbetering, de zogenaamde gerichte kwaliteitsverbetering. Daarom zouden nationale organisaties van cardiologen en cardiologieverpleegkundigen trainingen aan kunnen bieden aan zorgverleners in gerichte kwaliteitsverbetering.

- **Onderzoek vakgroepcompetenties en duurzaamheid van kwaliteitsverbetering**

Een vakgroep van goede individuen maakt nog geen goede vakgroep. Daarom kan het van meerwaarde zijn om een raamwerk te ontwikkelen voor goede vakgroepen. Daarnaast dient kwaliteitsverbetering geborgd te worden. Dit vraagt om verder onderzoek naar duurzame kwaliteitsverbetering.

- **Verbeter de richtlijnontwikkeling en adaptatie binnen de cardiologie**

Tot slot zijn de VMS ACS kwaliteitsindicatoren gebaseerd op de Europese cardiologie richtlijnen voor STEMI en NSTEMI & IAP. Echter, de ontwikkeling van deze richtlijnen voldoet niet volledig aan de huidige kwaliteitsstandaarden voor richtlijnontwikkeling. In aanvulling daarop adopteert de NVVC deze richtlijnen, waarbij ruimte voor verbetering is in het proces van adopteren en tevens adapteren.

DANKWOORD

Voor alle mensen die altijd geïnteresseerd hebben gevraagd hoe ver het stond met mijn promotie: ik ben blij nu te kunnen zeggen: klaar! Ondanks dat alleen mijn naam voor dit boekje staat, was dit nooit mogelijk geweest zonder de bijdragen van velen.

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Daarnaast natuurlijk mijn copromotoren, Martine en Ineke. Martine, je hebt me erg veel geleerd over dat onderzoek een balans is tussen strenge methodologie en praktische mogelijkheden. Je enthousiasme wist je altijd goed over te brengen op anderen, wat bij werving van ziekenhuizen erg handig was. Je dacht altijd in mogelijkheden en zelden in barrières, waardoor je soms een ware ideeënfontein was.
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Josien, we zijn in 2012 samen aan een promotietraject begonnen met allebei onze eigen focus. Het eerste punt was om als een bezetene de dataverzameling voor het dossieronderzoek op te zetten. Je gestructureerde manier van werken en doorzettingsvermogen waren een inspiratie. Ik heb zelden twee bureaus gezien die meer van elkaar verschilden dan de onze; de jouwe keurig opgeruimd, de mijne

bezaaid met onderzoekspapers. Ik ben er van overtuigd dat je een grote toekomst in het (verpleegkundig) onderzoek tegemoet gaat!

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